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The Assignment of Infrared Absorption Bands of p-Dichlorobenzene

By Shinnosuke SAËKI*

(Received December 27, 1959)

Many works have been published by a number of investigators concerning the vibrational spectra of *p*-dichlorobenzene (for example Ref. 1 and 2). But all of these measurements were done in solid state or in solution, and we have not yet any molecular spectrum of this substance in gaseous state. Since the spectrum of *p*-dichlorobenzene in solid or solution shows many strong overtones and combination liable to lead to an erroneous assignment, we have measured the gaseous spectra of deuterated and non-deuterated *p*-dichlorobenzenes to obtain the correct assignment.

Experimental

The measurements were carried out using Perkin-Elmer model 112 spectrometer, for the region from 5,000 to 2,000 cm^{-1} with a LiF prism, from 2,000 to 700 cm^{-1} with an NaCl prism and from 700 to 400 cm^{-1} with a KBr prism.

As the boiling points of these substances are considerably high (173.4°C for $C_6H_4Cl_2$), it was necessary to use a high temperature cell to obtain their gaseous spectra. An ordinary gas cell 85 mm. thick with pyrex bracelets of 15 mm. height on the KBr windows was coiled by a fine nichrome wire, then covered by a thick layer of asbestos for the sake of thermal insulation. The bracelets prevented the sample gas from condensing on the KBr windows and made sure to obtain the real gas phase spectra. This cell was usable at any temperature below 300°C by the aid of a slide wire resistor. We did not use any binding agent either to fix the KBr windows to the cell body, or to attach the pyrex rings to the windows, in order to avoid introduction of any impurity which might result from the thermal decomposition of the binding agent. The design of the cell is shown in Fig. 1. The inequality of the diameters at both ends of the cell might cause an inhomogeneity of the temperature in the cell to some extent, but it was not considered to have any effect on the spectra obtained.

The powder of the substance was put in the cell which was previously heated to a temperature sufficiently higher than its boiling point, and the measurement was carried out for the mixture of the vapor and the air at one atmospheric pressure.

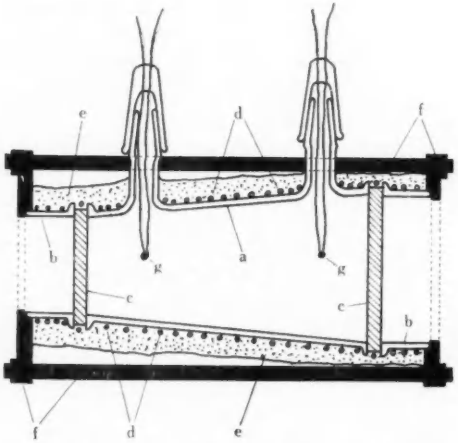

Fig. 1. Description of the high temperature cell

a: cell body
b: bracelets
c: KBr windows
d: nichrome wire
e: asbestos
f: supporting frame work
g: thermocouples

Results

The spectra obtained are shown in Fig. 2, and the observed frequencies of the absorption bands are shown in Table I. The spectra of deuterated *p*-dichlorobenzene were not so clear as those of ordinary *p*-dichlorobenzene because of the small available quantity of the substance. Thus we could detect no overtone nor combination band of deuterated *p*-dichlorobenzene

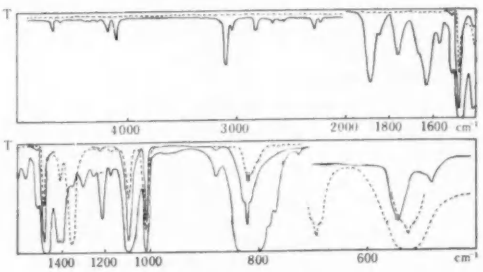

Fig. 2. Infrared absorption spectra of *p*-dichlorobenzene
—— non-deuterated
---- deuterated

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1) D. H. Whiffen, *Spectrochim. Acta*, **7**, 253 (1955).
2) E. K. Plyler, H. C. Allen, Jr. and E. D. Tidwell, *J. Research Natl. Bur. Standards*, **58**, 255 (1957).

TABLE I. OBSERVED FREQUENCIES (cm^{-1})

Non-deuterated		Deuterated	Non-deuterated		Deuterated	
4675	m		1626	s	1479	s
4605	w		1567	m		
4384	w		1509	m		
4328	w		1478	s	1404	m
4258	w		1417	s		
4170	m		1395	s	1357	s
4095	m		1348	w		
3094	s	(2290)	1301	m		
3035	m	(2283)	1251	w	1174	w
2816	m		1217	m	1090	s
2665	w		1175	w		
2590	w		1091	s	1020	s
2556	w		1014	s	800?*	m
2273	w		878	w		
2220	w		819	s	695	s
1882	s		725	w		
1837	w		544	s	526	s
1758	m		483	s	(436)	
1664	w				(414)	

N. B. The values in the brackets are the frequencies observed in solid state by other author (J. Lecomte, unpublished).
The indication of the intensities are not very precise.

* This band was covered by the strong band at 819 cm^{-1} of ordinary *p*-dichlorobenzene, and observed as a shoulder.

in the LiF region, and further it is necessary to mention here that the shapes of bands of deuterated *p*-dichlorobenzene in the figure are not so precise as those of ordinary *p*-dichlorobenzene.

Several measurements were repeated for non-deuterated *p*-dichlorobenzene to observe the correct shapes of the absorption bands, but were not successful except for those in the lower frequency part of NaCl region, that is, for the bands at 1013 cm^{-1} and at 819 cm^{-1} which were found to be type B and type C (or A) bands respectively. The other bands did not show any definite feature of the envelopes by which the types of the bands might be decided.

Assignment

The molecular structure of *p*-dichlorobenzene has the V_h symmetry, and we can expect for the molecule thirteen infrared active fundamental vibrations which are shown in Table II. Among those vibrations the frequencies of the C–Cl deformation vibrations are obviously too low to be measured under our experimental conditions, and it is possible that the frequencies of the ring deformation vibrations are also too low to be observed. Consequently only from nine to eleven bands are expected to be observed by our measurements.

TABLE II. INFRARED ACTIVE NORMAL VIBRATIONS OF *p*-DICHLOROBENZENE

Species B_{1u} (in-plane)
- C–H stretching
- C–H bending
- C–C stretching
- ring deformation
- C–Cl stretching

Species B_{2u} (in-plane)
- C–H stretching
- C–H bending
- C–C stretching
- ring deformation
- C–Cl deformation

Species B_{3u} (out-of-plane)
- C–H bending
- ring deformation
- C–Cl deformation

TABLE III. ASSIGNMENT OF INFRARED FUNDAMENTAL BANDS OF *p*-DICHLOROBENZENE

Species	Non-deuterated cm^{-1}	Deuterated cm^{-1}	Mode
B_{1u}	3094	2290	C–H stretching
	1478	1404	ring stretching
	1217	1090	C–H deformation
	1091	1020	skeletal vibration
	483	414	skeletal vibration
B_{2u}	3035	2283	C–H stretching
	1626	1479	ring stretching
	1405*	1357	C–H deformation
	1014	800	ring deformation
	—	—	C–Cl deformation
B_{3u}	819	695	C–H deformation
	544	526	ring deformation
	—	—	C–Cl deformation

N. B. Concerning the notations for symmetry species, we remark that we have chosen x-axis to be perpendicular to the plane of molecule and z-axis in the direction of the line combining two chlorine atoms.

* The mean value of 1395 and 1417 cm^{-1} in Table I.

We can easily assign the absorption bands at 3094 cm^{-1} (2290 cm^{-1} for $C_6D_4Cl_2$) and 3035 cm^{-1} (2283 cm^{-1} for $C_6D_4Cl_2$) to the two C–H (or C–D) stretching frequencies. The absorption band at 819 cm^{-1} of $C_6H_4Cl_2$ (695 cm^{-1} for $C_6D_4Cl_2$) is assigned to the out-of-plane vibration of C–H (or C–D) by many authors (for example, by D. H. Whiffen[2] and Y. Kakiuchi[3]). We have assigned a strong band at 544 cm^{-1} of $C_6H_4Cl_2$ (526 cm^{-1} for $C_6D_4Cl_2$) to the out-of-plane vibration of benzene ring. This band might be assigned to the in-plane deformation vibration of the ring.

3) Y. Kakiuchi, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **77**, 1572 (1956).

but, as shown later, this assignment does not satisfy the product rule.

As for the other normal frequencies, we measured seven strong bands between 1000 and 2000 cm^{-1} in the spectrum of $C_6H_4Cl_2$ (six bands for $C_6D_4Cl_2$), while there remain six normal vibrations to assign them. As there were too many absorption bands in the spectrum of $C_6H_4Cl_2$, we assumed that the two bands at 1417 and at 1395 cm^{-1} are caused by a Fermi resonance between a fundamental and a combination* near by it. Taking into account of the fact that the intensities of these two bands were nearly equal, we estimated that the position of the fundamental would be 1405 cm^{-1} (mean value of these two observed frequencies) if it were not for the Fermi resonance. We assigned the highest two of these six bands to the stretching vibrations of the ring, and the next two frequencies (one of which is the above-mentioned 1405 cm^{-1}) to the in-plane bending vibrations of C-H, and 1015 cm^{-1} and 1091 cm^{-1} to the deformation vibration of the ring and the stretching vibration of C-Cl respectively. As for the C-Cl stretching vibration, we could easily imagine from its abnormal frequency that this mode might be extremely mixed with some other modes. Although assignments of the last two frequencies seem to be mutually exchangeable, the exchange would result the larger deviation from the product rule.

In addition to the above-mentioned bands, we observed a strong band at 483 cm^{-1} in the spectrum of the $C_6H_4Cl_2$. This band corresponds to the band at 414 cm^{-1} in the spectrum of the $C_6D_4Cl_2$. We assigned these bands to the skeletal vibration of the molecule, i. e., the mixed vibration of ring deformation and C-Cl stretching.

Thus we assigned eleven of thirteen fundamental vibrations, and the remaining two fundamentals are the vibrations of C-Cl deformation, the frequencies of which are expected to be too low to be measured. The present assignments are shown in Table III.

Discussion

According to the product rule, the ratio of the products of the frequencies of non-deuterated and deuterated *p*-dichlorobenzene is 1.972 for the species B_{1u} and B_{2u}, and 1.388 for the species B_{3u}. In the case of the species B_{1u} we found that the ratio calculated from the observed frequencies was 1.970 which is in good accordance with the theoretical value. But in the case of the other species, the unobserved bands of low frequencies prevented us from applying the product rule perfectly, and all that we were able to do was to verify that the ratios calculated from the observed frequencies alone did not exceed the theoretical value. Actually these ratios were calculated as 1.917 and 1.219 for species B_{2u} and B_{3u} respectively, and these were quite plausible values.

As for the band envelopes, as mentioned in the previous chapter, for non-deuterated *p*-dichlorobenzene the band at 1014 cm^{-1} was found to be a type B band showing an apparent absorption minimum at the center of the band, while the band at 819 cm^{-1} was found to be type A or C band showing a prominent Q branch accompanied by P and R branches at its both sides. Considering that the axis of the largest moment of inertia of this molecule is perpendicular to the molecular plane, and that the axis of the smallest moment of inertia combines the two chlorine atoms, it would be easily shown that the type A, B and C bands belong to the species B_{1u}, B_{2u} and B_{3u} respectively, and that the band at 1014 cm^{-1} belongs to species B_{2u} and the band at 819 cm^{-1} belongs to the species B_{1u} or B_{3u}. The assignment shown in Table III is in good accordance with these results. The observed envelopes of the other bands were not adequately clear to give some suggestions for their assignments. Further for the spectra of deuterated *p*-dichlorobenzene we could not find any absorption band which showed a clear band envelope. The band at 819 cm^{-1} the envelope of which showed a clear feature of type A or C band was apparently to be considered as the extremely strong band of ordinary *p*-dichlorobenzene contained in deuterated *p*-dichlorobenzene as a slight impurity.

We had tried many other assignments which seemed to be compatible with the empirical knowledge. But they did not satisfy the product rule so well as the one shown in Table III.

The present assignment is different at some points from those given by other authors for their spectra in solid state or in solution. Comparing our gaseous spectra with those spectra of solid or solution, we saw that many strong bands in the latter spectra disappeared entirely or partially in the former. Thus we believe that the spectrum measured in solid state or in solution is not suitable for the assignment of the absorption bands.

Summary

The infrared absorption spectra of deuterated and non-deuterated *p*-dichlorobenzene were measured in the vapor state using a high

* We observed a strong Raman line at 331 cm^{-1}. The combination of this vibration with the infrared active vibration at 1090 cm^{-1} would appear in the neighborhood of 1405 cm^{-1}. We shall present a paper on the Raman spectra of *p*-dichlorobenzene in near future.

temperature cell. The results obtained by the measurements permitted us the assignment of the observed fundamental bands with the aid of the product rule. For some frequencies which we could not measure under our experimental conditions, we used the frequencies observed by other workers in the solid state which enabled us to apply the product rule.

This work was done at the laboratory of Professor J. Lecomte of the Laboratoire des Recherches Physiques, Faculté des Sciences de Paris. The author acknowledges gratefully his encouragement and advice. He also wishes to thank Dr. Leitch of the National Research Council at Ottawa for kindly sending us deuterated *p*-dichlorobenzene prepared by him.

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Faculté des Sciences de Paris

The Assignment of Infrared Absorption Bands of 1, 3, 5-Trichlorobenzene

By Shinnosuke SAËKI*

(Received January 23, 1960)

Several works have been published concerning the infrared spectra of 1, 3, 5-trichlorobenzene (for example, Ref. 1 and 2). However, all of these spectra were measured in solid state or in solution and we have no spectrum of this substance in vapor state. As we pointed out in our previous paper[3] chlorobenzenes show strong bands of overtones and combinations in solid state or in solution. So, one must be very cautious in trying the assignment of infrared bands of these substances using the spectra in these states. For this reason, we measured the infrared absorption spectra of deuterated and non-deuterated 1, 3, 5-trichlorobenzenes in vapor state to make the assignment of the absorption bands of these substances.

Experimental and Results

Spectral data were obtained by means of a Perkin-Elmer 112 spectrometer equipped with LiF, NaCl and KBr prisms. The measurements were carried out under ordinary pressure at high temperature. In these measurements we used the high temperatures cell which we described in detail in our previous paper[3]. The non-deuterated 1, 3, 5-trichlorobenzene used in our experiments was the "extra pure" one on the market, and the deuterated one was kindly provided by Dr. Leitch in Canada.

For the non-deuterated substance we made several measurements in various concentrations to obtain the correct frequencies and shapes of the strong bands and also to ascertain the existence of very weak bands. But, for the deuterated substance, we could not measure its spectra so attentively because of the smallness of the quantity, and it is possible that some weak bands were missed in our measurements. However, as we are going to assign only the fundamental bands of these spectra, this missing would not be very serious.

The spectra obtained by our measurements are shown in Fig. 1, and the frequencies of the observed bands are shown in Table I.

TABLE I. THE INFRARED ABSORPTION BANDS OF 1, 3, 5-TRICHLOROBENZENE (cm^{-1})

Non-deuterated		Deuterated		Non-deuterated		Deuterated	
4650	w	4550	w	1565	s	1549	s
4365	w	3256	w	1464	w		
4236	w	3105	w	1419	s	1333	s
4085	m	2800	w	1380	m	1257	m
3132	w	2687	w			1206	m
		2600	w	1261	w	1066	w
3089	m	(2310)				1024	w
2951	w	2274	w			950	w
2928	w					896	w
2838	w			1100	s		
2712	w			1055	m		
2632	w			889	w		
2592	m			853	s	843	s
2197	w			813	s	795	s
1944	w					769	w
1722	m			719	w		
1606	w			662	s	532	s

N. B. The value in the bracket is the frequencies observed in solid state by other authors. The indication of the intensities are not very precise.

* Present address: Government Chemical Industrial Research Institute, Tokyo. Hatagaya, Shibuya-ku, Tokyo.

1) E. Herz, K. W. F. Kohlrausch and R. Vogel, *Monatsh.* **76**, 200 (1947).
2) E. K. Plyler, H. C. Allen, Jr. and E. D. Tidwell, *J. Research Nat. Bur. Standards* **58**, 255 (1957).
3) S. Saëki, This Bulletin, **33**, 1021 (1960).

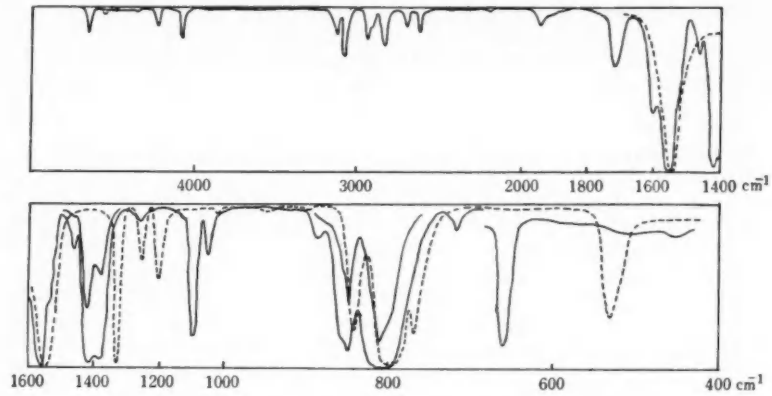

Fig. 1. Infrared absorption spectra of 1,3,5-trichlorobenzene.
—— non-deuterated ---- deuterated

Assignments

Assuming the molecular structure of 1,3,5-trichlorobenzene to be of D_{3h} form, it has ten infrared active fundamental frequencies, of which seven are doubly degenerate (species E′, in-plane) and three are non-degenerate (species A_2'', out-of-plane). The modes of these vibrations are shown in Table II. Of course we can not expect to observe all of these ten normal frequencies under our experimental conditions, because two C–Cl deformation frequencies (E′ and A_2'') are evidently too low to be measured, and two ring deformation frequencies might also exist below the observable region. Thus only from six to eight fundamental frequencies might be observed by our experiments. However, as is shown in Fig. 1 and Table I, there were too many strong bands in the spectra, but we could eliminate some of them by comparing the spectrum of non-deuterated substance with that of deuterated one.

Table II. Normal vibrations of 1,3,5-trichlorobenzene

E′ (in-plane)	A_2'' (out-of-plane)
C–H stretching	C–H deformation
ring stretching	ring deformation
ring stretching	C–Cl deformation
C–H deformation	
ring deformation	
C–Cl stretching	
C–Cl deformation	

We could easily assign the band at 3089 cm^{-1} of $C_6H_3Cl_3$ to the C–H stretching vibration (E′). The C–D stretching vibration of $C_6D_3Cl_3$ was not observed. It might be because of the unfortunate overlapping with the strong band of carbon dioxide near 2200 cm^{-1}. In solid state, it was observed at 2310 cm^{-1} [4].

We assigned two strong bands at 1565 and 1419 cm^{-1} of $C_6H_3Cl_3$ (1549 and 1333 cm^{-1} of C_6D_3Cl) to the ring stretching fundamental vibrations of species E′, and the strong band at 1380 cm^{-1} of $C_6H_3Cl_3$ to the C–H deformation vibration of E′ (in-plane). However, for the corresponding band of $C_6D_3Cl_3$, we observed two bands of considerable intensity at 1257 and 1206 cm^{-1}. These two bands were considered to be brought about by a Fermi resonance between a fundamental and an overtone or combination of species E′, and their nearly equal relative intensities suggested to us that the proper frequency of the concerned fundamental band might be about 1230 cm^{-1}. As for the overtone or combination band which interacts with the fundamental, we can say little of it because of the lack of data in the low frequency region and also of the lack of the Raman spectrum* of this substance.

We observed another strong band at 1100 cm^{-1} in the spectrum of $C_6H_3Cl_3$ but in the spectrum of $C_6D_3Cl_3$ we did not find any strong band corresponding to it. Although the intensity of the band at 1100 cm^{-1} of $C_6H_3Cl_3$ was very remarkable, this lack of corresponding band in the spectrum of $C_6D_3Cl_3$ kept us from assigning the band to a fundamental one.

The band at 853 cm^{-1} of $C_6H_3Cl_3$, was hitherto pointed out by many investigators[5] as an out-of-plane fundamental vibration band of C–H

4) J. Lecomte, unpublished.

* We have not yet succeeded in observing the Raman lines of this substance. For, when this substance was resolved in the solvents, the solution was slightly colored, and it prevented us from measuring the Raman spectrum.

5) For example, Y. Kakiuchi, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **80**, 356 (1959) and A. R. H. Cole and H. W. Thompson, *Trans. Faraday Soc.*, **46** 103 (1950).

bond. But, as is shown in our spectrum of Fig. 1, this band corresponds to the band at 843 cm^{-1} of $C_6D_3Cl_3$. That means, the frequency shift caused by the substitution of hydrogen atoms by deuterium atoms was only 10 cm^{-1}. If this is a band principally concerning the vibration of C–H bond, the frequency shift might be much greater than 10 cm^{-1}. Even if we dare to consider that it is the band at 769 cm^{-1} of $C_6D_3Cl_3$ that corresponds to 853 cm^{-1} of $C_6H_3Cl_3$, another difficulty would be caused. As we shall show later, we have a band in a lower frequency region which showed a large frequency shift by the substitution of hydrogen atoms, that is, the band at 662 cm^{-1} of C_6H_3 (532 cm^{-1} of $C_6D_3Cl_3$). If we assign the band at 853 cm^{-1} to the out-of-plane C–H vibration, there should be no way to explain the band at 662 cm^{-1} which was shifted widely to 532 cm^{-1} by the introduction of deuterium atoms. Therefore we did not assign this band at 853 cm^{-1} (at 843 cm^{-1} in the case of $C_6D_3Cl_3$) to the out-of-plane C–H (or C–D) vibration. One might also assign it to the in-plane ring deformation fundamental vibration (E′). But it is generally known that the frequency of this mode is very variable over a wide region, especially when there is a large possibility of coupling with other modes. So we are not sure that we could assign this band to the ring deformation fundamental vibration. After all we assigned it to no normal vibraton. After all we assigned it to no normal vibration, considering it as an overtone or combination band which was brought about by the Fermi resonances with a fundamental band at 813 cm^{-1} and which borrowed the intensity from the fundamental band. Thus we could get over the superabundance of the strong bands in the observed spectra.

We assigned the very strong bands at 813 cm^{-1} of $C_6H_3Cl_3$ and at 795 cm^{-1} of $C_6D_3Cl_3$ to the C–Cl stretching vibration. But it should be mentioned here that this designation of the vibrational mode is used just as a convention. For, as we showed in our previous paper[3], the mixing of the vibrational modes is extreme in this region of frequency, and it might not be very correct to designate the modes of these normal vibrations by simple terms as C–Cl stretching vibration and so forth.

We observed only one strong band in KBr region in each spectrum of $C_6H_3Cl_3$ and $C_6D_3Cl_3$, that is, the bands at 662 cm^{-1} and at 532 cm^{-1} respectively. As there was no other strong absorption band, it is quite certain that these two bands correspond to each other. Further, the fact that the ratio of their frequencies is considerably apart from 1 (1.24) suggests to us that these vibrational bands are concerned with the hydrogen and deuterium atoms respectively. For the spectrum of mesitylene Whiffen[6] assigned the band at 928 cm^{-1} to the out-of-plane vibration of C–H bond. In the case 1, 3, 5-trichlorobenzene, since no appropriate strong band was found in the neighbourhood of 900 cm^{-1}, we assigned the band at 662 cm^{-1} (at 532 cm^{-1} for $C_6D_3Cl_3$) to the C–H (C–D) out-of-plane vibration. The above-mentioned assignment is shown in Table III.

TABLE III. THE ASSIGNMENT OF THE INFRARED BANDS OF 1, 3, 5-TRICHLOROBENZENE

Type	$C_6H_3Cl_3$	$C_6D_3Cl_3$	Mode
E′	3089	(2310)	C–H stretching
	1565	1549	ring stretching
	1419	1333	ring stretching
	1380	1230*	C–H deformation
	813	795	C–Cl stretching
	—	—	ring deformation
	—	—	C–Cl deformation
A_2''	662	532	C–H deformation
	—	—	ring deformation
	—	—	C–Cl deformation

* This is the average value of the two observed frequencies, i.e., 1257 and 1206 cm^{-1}.

Discussion

The theoretical values of the ratios of products of normal frequencies of each substance (deuterated and non-deuterated) are 1.972 for the species E′ and 1.402 for the species A_2''. For the species A_2'' we could observe only one frequency of each substance, and it was impossible to apply the product rule to this species. The only one observed frequency of species A_2'' was 662 cm^{-1} of $C_6H_3Cl_3$ (532 cm^{-1} of $C_6D_3Cl_3$) which we assigned to the out-of-plane C–H (or C–D) fundamental vibration by reason of the large shift of frequency accompanying the substitution of hydrogen atoms by deuterium atoms. As was mentioned in the previous section, this assignment is quite different from that which is generally admitted now. We can not get to a definite conclusion on this point at present, but if we succeed in measuring the spectra of these substances in the far infrared region, and if we observe the other two out-of-plane fundamental bands, we shall be able to determine the correct assignment.

For the species E′ too, there were some frequencies that were left unobservable under our experimental conditions, and it is also impossible to apply the product rule perfectly. But, in this case, five or six normal frequencies (seven in all) were observed, so it is not

6) D. H. Whiffen, *Spectrochim. Acta*, 7, 253 (1955–6).

completely meaningless to calculate the ratio of products of observed frequencies alone. This calculated ratio was 1.650, when we excluded the pair of frequencies at 853 cm^{-1} (for $C_6H_3Cl_3$) and at 843 cm^{-1} (for $C_6D_3Cl_3$) from this calculation. It means that the ratio of products by the other two unobserved frequencies is to be about 1.19, and this is quite an appropriate value. But if we include the above-mentioned pair of frequencies into this calculation, the ratio increases only a little and becomes 1.670. It requires that the ratio of the last unobserved frequency of each substance is 1.18. This value seems to be too great to attribute to the ratio of only one pair of frequency. This is another reason why we have not dared to assign this pair of bands to the fundamental ones.

Summary

The infrared absorption spectra of deuterated nd non-deuterated 1,3,5-trichlorobenzenes were measured in the vapor state from 5,000 to 400 cm^{-1}. The results of our measurements allowed us the assignment of the fundamental bands of this substance by the aid of the product rule. As we could not observe all of the fundamental bands of this substance, the perfect application of the product rule was not possible. But we proved that our assignment did not conflict with the product rule.

This work was done at the laboratory of Professor J. Lecomte of the laboratoire des Recherches Physiques, Faculté des Sciences de Paris. The author acknowledges gratefully Professor Lecomte's encouragement and advice. He also wishes to thank Dr. Leitch of the National Research Council at Ottawa for kindly sending deuterated 1, 3, 5-trichlorobenzene prepared by him.

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The n—π Transition Band of Acenaphthenequinone*

By Akira KUBOYAMA

(Received January 26, 1960)

In a previous paper[1], Nagakura and the present author measured the weak visible bands of *o*- and *p*-quinones in various solvents. From the result on the solvent effect these bands were ascribed to an $n-\pi^*$ transition, namely, the transition from the non-bonding electron orbital of oxygen atom to the excited π-electron orbital. However, the $n-\pi^*$ transition band of acenaphthenequinone has never been studied. Thus, the present author measures the $n-\pi^*$ transition band of acenaphthenequinone in various solvents. Further, for the purpose of comparison, the absorption spectra of various *o*- and *p*-quinones are newly measured. The obtained results are now reported.

Experimental

Measurements. — The absorption spectra were measured with a Cary recording spectrophotometer 14 M. Quartz cylindrical cells with path lengths of 1, 2 and 5 cm. were used. A thermostated cell jacket was used for measurements at 35°C.

Materials. — Acenaphthenequinone[2] (AQ) was prepared through the oxidation of acenaphthene with potassium bichromate and was recrystallized from benzene, m. p. 256°C. *p*-Benzoquinone[3] was prepared through the oxidation of hydroquinone with potassium bichromate and was purified by sublimation, m.p. 114°C. α- And β-naphthoquinones and phenanthrenequinone were prepared according to L. F. Fieser's method[4]. α-Naphthoquinone was purified by charcoal treatment in ether solution, m. p. 124°C. β-Naphthoquinone was used without further purification, according to Fieser's note[4], m. p. with decomp. 145~147°C. Phenanthrenequinone was recrystallized from ethanol, m. p. 208°C. All the solvents used in the present study were of special grade. Benzene and ethyl ether were distilled after being dried over sodium metal. Dioxane was distilled from sodium metal, after being dried with it. Carbon disulfide was distilled after being dried over calcium chloride, and was

1) S. Nagakura and A. Kuboyama, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **74**, 499 (1953); S. Nagakura and A. Kuboyama, *J. Am. Chem. Soc.*, **76**, 1003 (1954).

2) "Organic Syntheses", Vol. XXIV, p. 1.

3) "Organic Syntheses", Col. Vol. I, p. 469.

4) L. F. Fieser, "Experiments in Organic Chemistry", D. C. Heath and Co., Boston (1941), pp. 230, 232 and 233.

kept in the dark. Chloroform was washed successively with concentrated sulfuric acid and with aqueous sodium hydroxide, and was distilled after being dried over calcium chloride. *n*-Heptane was distilled after being treated as in the case of chloroform and being dried over sodium metal.

Results

The obtained absorption spectra are given in Figs. 1—6. The spectra of AQ in various solvents are given in Figs. 1* and 2 and those of β-naphthoquinone, phenanthrenequinone, *p*-benzoquinone, and α-naphthoquinone are given in Figs. 3**, 4, 5 and 6, respectively.

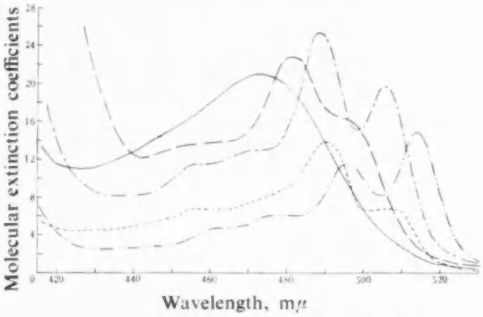

Fig. 1. Absorption spectra of acenaphthenequinone, solvent, —— benzene, —— chloroform, —— dioxane, —— carbon disulfide, —— ethyl ether (in case of the latter two*, the scale of the ordinate is arbitrary).

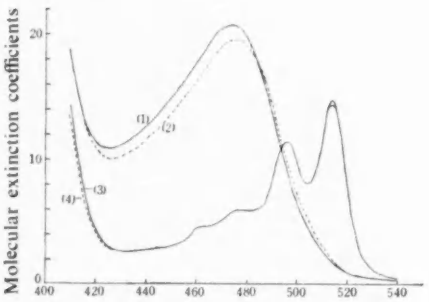

Fig. 2. Absorption spectra of acenaphthenequinone, solvent, (1), (2) dioxane, (3), (4) carbon disulfide; temperature, (1), (3) room temperature (17°C), (2), (4) 37°C (in case of carbon disulfide, the scale of the ordinate is arbitrary).

*1 AQ is sparingly soluble in carbon disulfide and ethyl ether. Thus, the molecular extinction coefficient of the α-band in these solvents could not be determined.

2 The longest wavelength π-π transition band of β-naphthoquinone in chloroform largely shifts towards longer wavelengths as in AQ.

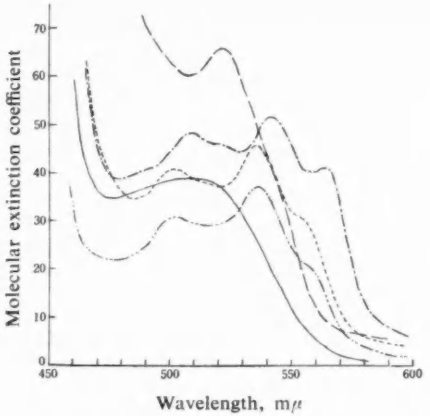

Fig. 3. Absorption spectra of β-naphthoquinone, solvent; —— carbon disulfide, —— benzene, —— ethyl ether, —— chloroform, —— dioxane.

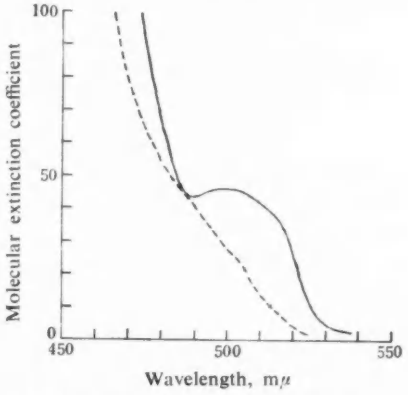

Fig. 4. Absorption spectra of phenanthrenequinone, solvent; —— benzene, —— dioxane.

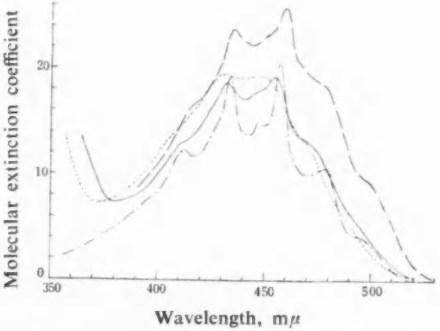

Fig. 5. Absorption spectra of *p*-benzoquinone, solvent; —— carbon disulfide, —— *n*-heptane, —— benzene, —— dioxane.

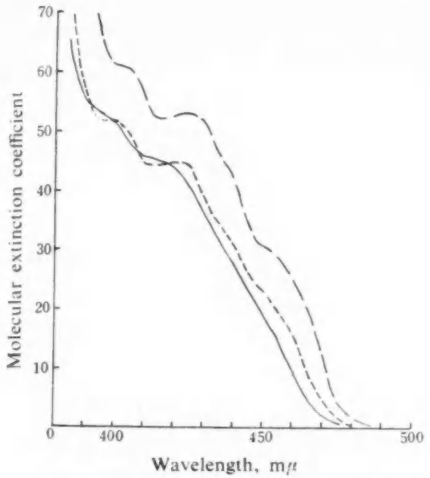

Fig. 6. Absorption spectra of α-naphthoquinone, solvent; —— carbon disulfide, ---- benzene, —— dioxane.

Discussion

In the visible and near UV regions, AQ has three main peaks at 225 mμ, 300 mμ, and 500 mμ. It is thought that strong peaks at 225 mμ and 300 mμ correspond to the β and the p bands of naphthalene[5], respectively, while a weak peak at 500 mμ which is given in Fig. 1 is assumed to be an $n-\pi^*$ transition band from the consideration of its intensity and position. Hereafter, this band will be called the α-band. As for the solvent effect on the α-band, which is shown in Fig. 1, two points are noticeable. First, the α-band in dioxane and chloroform largely shifts towards shorter wavelengths and almost completely loses vibrational structures. Secondly, the relative height of the two main peaks of the α-band markedly depends upon solvents such as carbon disulfide, benzene, ethyl ether etc. As for the first point, the blue-shift of the α-band in chloroform is attributed to hydrogen bond formation[6]. This fact verifies the assignment of the α-band to the $n-\pi^*$ transition band. The large blue-shift of the α-band in dioxane may be attributable to molecular complex formation. Here, dioxane is an n-type donor[7]. The blue-shift of an $n-\pi^*$ transition band due to molecular complex formation has never been pointed out. The mechanism of this blue-shift is thought to be similar to the one[8] due to the substitutions of electron-donating groups to a π-electronic system containing carbonyl groups. The fact that such a large blue-shift of the α-band as in dioxane is not seen in ethyl ether, may be attributable to the large steric hindrance caused by the side chains of ethyl ether in the molecular complex formation. As is seen from Figs. 1, 3, 4, 5 and 6, the blue-shift of the α-band in dioxane is much larger in the ortho-type quinones than in the para-type quinones***. This fact may be explained as follows. The oxygen atoms of dioxane are expected to coordinate themselves to carbon atoms of carbonyl groups of the quinones by the electrostatic interaction as well as by the charge transfer interaction. The electrostatic interaction is thought to be caused by the interaction between the atomic dipoles of the oxygen atoms of dioxane and the positive charges of the carbon atoms of the carbonyl groups. Hence, the magnitude of the electrostatic interaction is determined by the amount of the positive charges of the carbon atoms. The charge transfer interaction can be approximately represented by the interaction between the lowest unfilled orbitals of the quinones and the lone pair orbitals of the oxygen atoms of dioxane. Therefore, the magnitude of the charge transfer interaction is roughly determined by the coefficients of the atomic orbitals of the carbonyl carbon atoms in the lowest unfilled orbitals of the quinones. The greater those coefficients are, the greater is the charge transfer interaction. From our previous calculations[9] for o- and p-quinones, it is seen that the above two requirements are best fulfilled by the carbon atoms of the carbonyl groups of the quinones. The above requirements are also expected to be satisfied for AQ, which may be regarded as one of the o-quinones. Since in o-quinones the two carbon atoms of the two carbonyl groups are jointed with each other, the interaction between the oxygen atoms of dioxane and the carbonyl carbon atoms of o-quinones**** is expected to be larger than that of p-quinones. It is naturally expected that the above fact is ascribed to this point.

As for the second point previously described, there occurs a question whether the two main peaks of the α-band are ascribed to the vibrational structure of the one $n-\pi^*$ transition

5) E. Clar, "Aromatische Kohlenwasserstoffe" 1st Edn., Springer, Berlin (1941).
6) G. J. Brealey and M. Kasha, *J. Am. Chem. Soc.*, **77**, 4462 (1955).
7) R. S. Mulliken, *J. Chem. Phys.*, **56**, 801 (1952).
8) H. Baba, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **72**, 341 (1951); S. Nagakura, This Bulletin, **25**, 164 (1952).
*) Previously, L. S. Forster found that the weak visible absorption band of biacetyl in dioxane shows relatively large shift towards shorter wavelengths (*J. Am. Chem. Soc.*, **77**, 1417 (1955)). But this blue-shift is not so large as the ones of ortho-type quinones, here found.
9) a) A. Kuboyama, This Bulletin, **31**, 752 (1958); b) A. Kuboyama, ibid., **32**, 1226 (1959).

band, to the two different $n-\pi^*$ transition bands of the one form of AQ or to the two different $n-\pi^*$ transition bands belonging to the two different forms of AQ. As is seen in Fig. 2, the α-band in dioxane and in carbon disulfide are almost independent of temperature. Thus, the third possibility is probably denied. As is seen in Fig. 3, the behaviors of the two peaks in the longer wavelength side of β-naphthoquinone are, though less marked, similar to the ones of the two main peaks of the α-band of AQ and the distance (ca. 700 cm^{-1}) between the two peaks of β-naphthoquinone is almost equal to that of the α-band****. Previously, J. W. Sidman[10] experimentally concluded that *p*-benzoquinone in crystalline state has two distinct singlet-singlet $n-\pi^*$ transition bands in the wave number region of 20000 cm^{-1} to 25000 cm^{-1}. In that case, the wave number difference between the two 0–0 bands corresponding to these two transitions was determined to be 797 cm^{-1}. In connection with Sidman's conclusion mentioned above, it[11] may safely be assumed that the two main peaks of the α-band may be due to the two $n-\pi^*$ transitions whose energy difference is ca. 700 cm^{-1}.

As is seen in Figs. 3, 5 and 6, in carbon disulfide the intensities of the $n-\pi^*$ transition bands of the quinones, especially of *p*-benzoquinone, are considerably larger than the ones in the other solvents. This fact is probably attributed to the large refractive index of carbon disulfide[12].

Summary

The weak absorption band (α-band) ($\varepsilon_{max}\sim$ 20) near 500 mμ of acenaphthenequinone was measured in various solvents. This band was determined as the $n-\pi^*$ transition band on the basis of the observed results on intensity and solvent effect. In dioxane, the $n-\pi^*$ transition bands of the *o*-quinones, including the α-band, largely shift towards shorter wavelengths. This fact, which is thought to be due to molecular complex formation, was discussed from the qualitative point of view. The relative height of the two main peaks of the α-band markedly depends upon solvents. The similar, though less marked, fact is seen in β-naphthoquinone. The two main peaks of the α-band were assumed to be due to the two $n-\pi^*$ transitions, whose transition energy difference is ca. 700 cm^{-1}. It was found that the $n-\pi^*$ transition bands of the quinones, especially of *p*-benzoquinone, are markedly intensified in carbon disulfide. This fact is probably attributed to the large refractive index of this solvent.

The author wishes to express his sincere thanks to Professor S. Nagakura of the University of Tokyo for his kind guidance and to Dr. Y. Mashiko of this Institute for his kind offices. The author's thanks are also due to Mr. H. Takaya for his kind cooperation in this research.

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*** The signs of the two atomic orbitals of the two carbonyl carbon atoms in the lowest unfilled orbitals of *o*-quinones[9b] are equal.

**** Forster[11] found the fact, similar to the one of β-naphthoquinone, for the $n-\pi^*$ transition band of biacetyl, where the distance between the two peaks is ca. 1300 cm^{-1}. He thought that these two peaks respectively result from two electronic transitions.

10) J. W. Sidman *J. Am. Chem. Soc.* **78**, 2363 (1956).
11) H. L. McMurry, *J. Chem. Phys.*, **9**, 245 (1941).
12) N. Q. Chako, *J. Chem. Phys.*, **2**, 644 (1934).

The Stochastic Model for Unimolecular Gas Reaction

By Kenji ISHIDA

(Received July 13, 1959)

According to the probabilistic representation for the deterministic theory of the "true" unimolecular gas reaction[1], in which it is assumed that the reactant molecules are independent of the coexisting resultant molecules, i. e., the distribution of each reactant molecule is not correlated to the distribution of each resultant molecule, and that the reverse reaction is not taking place, the fraction of the reactant molecules which react during time dt can be set equal to the probability $k_1 dt$;

$$-\frac{dn}{n}=k_1 dt \qquad (1)$$

1) Jen-Yuan Chien, *J. Chem. Phys.*, **16**, 426 (1948). See, e. g., A. A. Frost and R. G. Pearson, "Kinetics and Mechanism", John Wiley & Sons, Inc., New York (1953), p. 67.

where the rate constant k_1 denotes the probability that one molecule reacts during unit time, n is the number of reactant molecules at time t and $-dn$ the number reacting during time dt. It should be emphasized, however, that in Eq. 1 the probabilistic notions are not manifested in a precise form, and that the number of molecules predicted for various times is not precise, but the reaction proceeds at random at an average rate[2]. In order to formulate this on the basis of the mathematically exact laws of the theory of probability, Bartholomay[3] has recently presented a method to construct the stochastic model for the true unimolecular gas reaction by starting from the deterministic theory as represented by Eq. 1. But the chemical and mathematical foundations on which the theory of the stochastic process can be applied to this chemical reaction do not appear to have been exactly mentioned. Therefore it is instructive to formulate definitely the probabilistic properties of the chemical reaction.

If the number of resultant molecules produced during the time interval $(0, t)$ is denoted by $n_p(t)$, the function $n_p(t)$ itself is a random variable for all arbitrary but fixed periods of duration t. Since the function $n_p(t)$ which assumes only the integers and is nondecreasing becomes the aggregate of random variables with continuous parameter when t varies, this represents a possible development of the chemical reaction. Consequently the course of the chemical reaction is a stochastic process. It has been acknowledged, in general, that under the given temperature and external parameters the rate of a chemical reaction is determined only by the composition of the reaction system at the time and does not depend on its previous history, so that it is concluded that the course of chemical reaction is a Markov process[4]. It has been recognized for many years that by its very nature a chemical reaction must disturb the equilibrium distribution of the reactant species[5]. If, however, we assume that the rate of the chemical reaction is sufficiently small compared with the rate of energy exchange and the disturbance of the equilibrium distribution of energy during the course of the chemical reaction can be approximately neglected, the reaction system can be discussed on the assumption that it is at thermal equilibrium. By "temporally homogeneous"[6] for the course of chemical reaction we mean that the thermal equilibrium remains absolutely unchanged throughout the process. Accordingly, we obtain the conclusion that *the theory of temporally homogeneous Markov process can be applied to the course of chemical reaction* for such reaction systems at thermal equilibrium that the reactant molecules do not interact mutually with the coexisting resultant molecules and the reverse reaction does not occur, and such conditions permit us to calculated the average rate of the chemical reaction at a time.

Although the one-dimensional stochastic process for the total number of reactant molecules has been studied by Bartholomay who, from the macroscopic point of view, has given a rate constant to the whole reaction, we shall be able to calculate the average rate constant by constructing microscopically the multi-dimensional stochastic process[7] for the number of reactant molecules in various states of energy, on the assumption that the stochastic model is conformable also to the "true" unimolecular reaction concerning the reactant molecules in each state of energy.

One-dimensional Stochastic Model

In general the Chapman-Kolmogorov equation for temporally homogeneous Markov processes[8] is given by

$$P_{i,n}(t+\tau)=\sum_{\nu}P_{i,\nu}(t)\cdot P_{\nu,n}(\tau) \qquad (2)$$

where $P_{i,\nu}(t)$ is the transition probability from any state E_i to any other state E_ν during the time interval of length t and for the process of chemical reaction i, ν and n represent the numbers of reactant molecules, respectively. If the initial probability $P_i(0)$ is known, then the probability $P_n(t)$ of finding the system at time t in the state E_n is set equal to the quantity $\sum_{i=0}^{n_0}P_i(0)P_{i,n}(t)$ according to the theorem of total probability[9], that is, $P_n(t)=\sum_{i=0}^{n_0}P_i(0)P_{i,n}(t)$, where n_0 is the total number of reactant molecules at time $t=0$. Hence this probability $P_n(t)$ is related to both t and $P_i(0)$. In our case, however, it may be provided that one of the probabilities $P_i(0)$ $(i=0, 1, 2, \cdots\cdots, n_0)$ is equal to one, and the others to zero;

$$\text{if} \qquad i=n_0, \quad P_i(0)=1 \qquad (3)$$

2) L. Pauling, "General Chemistry", W. H. Freeman and Co. (1949), p. 335.
3) G. F. Bartholomay, *Bull. Math. Biophys.*, **20**, 175 (1958).
4) W. Feller, "An Introduction to Probability Theory and its Applications", John Wiley & Sons, Inc., New York (1950), p. 337.
5) R. H. Fowler and E. A. Guggenheim, "Statistical Thermodynamics". Cambridge University Press (1939), p. 490.
6) W. Feller, Ref. 4, p. 386.
7) N. Arley, "On the Theory of Stochastic Process and their Application to the Theory of Cosmic Radiation", John Wiley & Sons, Inc., New York (1948), p. 73.
8) W. Feller's book, p. 388.
9) A. N. Kolmogorov, "Foundations of the Theory of Probability" (Translation edited by Nathan Morrison), Chelsea Publishing Co., New York (1950), p. 7.

otherwise, $P_i(0)=0$

Multiplying both sides of Eq. 2 by $P_i(0)$ and summing over all values of i, we get

$$\sum_{i=0}^{n_0} P_i(0)P_{i,n}(t+\tau)=\sum_{\nu}\left(\sum_{i=0}^{n_0} P_i(0)P_{i,\nu}(t)\right)P_{\nu,n}(\tau)$$

which is reduced to, according to the theorem of total probability,

$$P_n(t+\tau)=\sum_{\nu} P_\nu(t)P_{\nu,n}(\tau) \tag{4}$$

where $P_\nu(t)$ denotes the probability of finding ν reactant molecules at time t in the reaction system. This is the fundamental equation for the application of the stochastic process to the chemical reaction.

If at time t the reaction system is in the state E_n, the probability that any one of n reactant molecules will undergo a reaction during the infinitely small time interval of length $(t, t+\tau)$ is equal to $P_{n,n-1}(\tau)=k_1 n\tau+o(\tau)$, where k_1 is a constant and $o(\tau)$ denotes the probability that more than one reaction occurs is of smaller order of magnitude than τ. Similarly the transition probability $P_{n+1,n}(\tau)$ from the state E_{n+1} to the adjacent state E_n is equal to $k_1(n+1)\tau+o(\tau)$, and the probability of staying in the state E_n is given by $P_{n,n}(\tau)=1-P_{n,n-1}(\tau)=1-(k_1 n\tau+o(\tau))$. Rewriting $P_\nu(t)$ in the alternative form $P(\nu, t)$, we have, according to Eq. 4,

$$\begin{aligned}P(n, t+\tau)&=P(n+1, t)P_{n+1,n}(\tau)+P(n, t)P_{n,n}(\tau)\\&=k_1(n+1)\tau P(n+1, t)\\&\quad+(1-k_1 n\tau)P(n, t)+o(\tau)\end{aligned}$$

From this we obtain

$$\begin{aligned}\frac{P(n, t+\tau)-P(n, t)}{\tau}&=-k_1 nP(n, t)\\&\quad+k_1(n+1)P(n+1, t)+o(1)\end{aligned}$$

Thus if we let $\tau\to 0$ for fixed t, we have

$$\frac{\mathrm{d}}{\mathrm{d}t}P(n, t)=-k_1 nP(n, t)+k_1(n+1)P(n+1, t) \tag{5}$$

In particular, by assuming $P(n+1, t)=0$ for $n=n_0$, we obtain $\dfrac{\mathrm{d}}{\mathrm{d}t}P(n_0, t)=-k_1 n_0 P(n_0, t)$ in place of Eq. 5, and for $n=0$, Eq. 5 is reduced to $\dfrac{\mathrm{d}}{\mathrm{d}t}P(0, t)=k_1 P(1, t)$. Hence Eq. 5 holds for all values of n. Solving Eq. 5 under the conditions (3), we obtain the binomial distribution

$$P(n, t)=\binom{n_0}{n}\{\exp(-k_1 t)\}^n\{1-\exp(-k_1 t)\}^{n_0-n} \tag{6}$$

whose derivation will be shown later. Of course, the equation $\sum_{n=0}^{n_0}P(n, t)=1$ holds certainly.

In order to reduce Eq. 5 to the equation of the mean value for the number of reactant molecules, if we multiply both sides of Eq. 5 by n and summing over all values of n, we get

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n=0}^{n_0} nP(n, t)&=-k_1\sum_{n=0}^{n_0} n^2P(n, t)\\&\quad+k_1\sum_{n=0}^{n_0} n(n-1)P(n, t)\end{aligned}$$

that is,

$$\frac{\mathrm{d}\langle n\rangle}{\mathrm{d}t}=-k_1\langle n\rangle \tag{7}$$

where $\sum_{n=0}^{n_0} nP(n, t)=\langle n\rangle$ denotes the mean value for the number of reactant molecules at time t. This equation is consistent "in the mean" with the deterministic rate equation $\dfrac{\mathrm{d}n}{\mathrm{d}t}=-k_1 n$, excepting the chance fluctuations* which arise inherently in the reaction itself and are not associated with random experimental errors.

We have so far discussed the stochastic model for such a true unimolecular reaction as the rate constant k_1 is invariable with time, but we can easily extend this to the more general cases in which the rate constants are variable with time. Using in place of k_1 the "instantaneous" value $k(t)$ of the rate constant which is able to take different values at different points on the time axis, we have, instaed of Eq. 5,

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}P(n, t)&=-k(t)nP(n, t)\\&\quad+k(t)(n+1)P(n+1, t)\end{aligned} \tag{8}$$**

In order to solve this equation, we introduce the generating function $\varphi(t, x)=\sum_{n=0}^{n_0} x^nP(n, t)$, which is convergent for $|x|\leq 1$ and defined so that the coefficient of x^n is the probability of finding n reactant molecules at time t in the reaction system. Multiplying both sides of Eq. 8 by x^n and summing from $n=0$ to $n=n_0$, we have

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n=0}^{n_0} x^nP(n, t)&=-k(t)\sum_{n=0}^{n_0} nx^nP(n, t)\\&\quad+k(t)\sum_{n=0}^{n_0} nx^{n-1}P(n, t)\end{aligned}$$

Substituting $\dfrac{\partial\varphi}{\partial t}=\dfrac{\mathrm{d}}{\mathrm{d}t}\sum_{n=0}^{n_0} x^nP(n, t)$ and $x\dfrac{\partial\varphi}{\partial x}=\sum_{n=0}^{n_0} nx^nP(n, t)$ into this equation, we obtain the first-order partial differential equation

* cf. Eq. 22.

** This equation refers to non-stationary process with $k(t)$ depending on time. Since, however, Eq. 5 has the purely "localized" property, the method by which we have derived Eq. (5) is completely applicable to such Markov processes as are not temporally homogeneous.

$$\frac{\partial\varphi}{\partial t}=k(t)(1-x)\frac{\partial\varphi}{\partial x} \tag{9}$$

The auxiliary differential equation of Eq. 9 is given by

$$\frac{dx}{k(t)(1-x)}=\frac{\mathrm{d}t}{-1}$$

Solving this, we obtain

$$(1-x)\exp\left(-\int_0^t k(t)\mathrm{d}t\right)=\text{constant}$$

According to the theory of partial differential equation the general solution of Eq. 9 is then given by

$$\varphi(t,x)=f\left((1-x)\exp\left(-\int_0^t k(t)\mathrm{d}t\right)\right) \tag{10}$$

where f is an arbitrary function which is to be determined by the initial condition; the function f is led to the form $f(1-x)=x^{n_0}$ by $\varphi(0,x)=f(1-x)$ and $\varphi(0,x)=\sum_{n=0}^{n_0}x^nP(n,0)=x^{n_0}$, where the initial condition (3) has been used. If we replace $1-x$ by ξ, we obtain the relation $f(\xi)=(1-\xi)^{n_0}$. Again, replacing ξ by $(1-x)\exp\left(-\int_0^t k(t)\mathrm{d}t\right)$, we can transform Eq. 10 into the form

$$\varphi(t,x)=\left\{\left(1-\exp\left(-\int_0^t k(t)\mathrm{d}t\right)\right)+x\exp\left(-\int_0^t k(t)\mathrm{d}t\right)\right\}^{n_0} \tag{11}$$

which satisfies the condition $\varphi(t,1)=1$, i.e., $\sum_{n=0}^{n_0}P(n,t)=1$. Hence expanding the r. h. s. of Eq. (11), we obtain the binomial distribution by the definition of the generating function,

$$P(n,t)=\binom{n_0}{n}\left(\exp\left(-\int_0^t k(t)\mathrm{d}t\right)\right)^n\times\left(1-\exp\left(-\int_0^t k(t)\mathrm{d}t\right)\right)^{n_0-n} \tag{12}$$

Since the mean value for the number of reactant molecules at time t is given by $\langle n\rangle=\left(x\frac{\partial\varphi}{\partial x}\right)_{x=1}$, we can easily find

$$\langle n\rangle=n_0\exp\left(-\int_0^t k(t)\mathrm{d}t\right) \tag{13}$$

If $k(t)$ is set equal to k_1 invariable with time, the above equation becomes $\langle n\rangle=n_0\exp(-k_1t)$, which agrees with the integral of Eq. 7. Such stochastic processes with the variable parameter $k(t)$ can be applied to such various cases as will be described below.

Example 1. Bimolecular Reaction. — The deterministic rate of the bimolecular reaction $2A\rightarrow A_2$ is expressed in the form

$$\frac{\mathrm{d}(2n)}{\mathrm{d}t}=-k_2(2n)^2 \tag{1,1}$$

where $2n$ denotes the number of reactant molecules at time t and k_2 the rate constant. Solving Eq. 1,1 under the initial condition that $2n=2n_0$ at $t=0$, we obtain

$$2n=\frac{2n_0}{1+k_2(2n_0)t} \tag{1,2}$$

or if we set $2n=N$, this becomes

$$N=\frac{N_0}{1+k_2N_0t} \tag{1,3}$$

From Eq. 1,2 the probability that any one of n reactant molecules undergoes a chemical transformation during the time interval $(t, t+\Delta t)$ is given by

$$\frac{|\Delta n|}{n}=\frac{k_2N_0}{1+k_2N_0t}\Delta t+o(\Delta t) \tag{1,4}$$

If we set $\frac{k_2N_0}{1+k_2N_0t}=k(t)$, then we have according to Eq. 8

$$\frac{\mathrm{d}}{\mathrm{d}t}P(n,t)=-\frac{k_2N_0}{1+k_2N_0t}nP(n,t)+\frac{k_2N_0}{1+k_2N_0t}(n+1)P(n+1,t) \tag{1,5}$$

Multiplying both sides of Eq. 1,5 by n and summing over all values of n, we obtain as the differential equation concerning the mean value for the number of reactant molecules

$$\frac{\mathrm{d}\langle n\rangle}{\mathrm{d}t}=-\frac{k_2N_0}{1+k_2N_0t}\langle n\rangle \tag{1,6}$$

or

$$\frac{\mathrm{d}\langle N\rangle}{\mathrm{d}t}=-\frac{k_2N_0}{1+k_2N_0t}\langle N\rangle \tag{1,7}$$

whose solution is given by

$$\langle N\rangle=\frac{N_0}{1+k_2N_0t} \tag{1,8}$$*

* In general we have as the stochastic model for the bimolecular reaction $2A\rightarrow A_2$

$$\frac{\mathrm{d}}{\mathrm{d}t}P(2n,t)=-k_2\frac{(2n)(2n-1)}{2}P(2n,t)+k_2\frac{\{2(n+1)\}\{2n+1)-1\}}{2}P(2(n+1),t) \tag{1}$$

Transforming this into the differential equation of the mean value, we obtain

$$\frac{\mathrm{d}\langle 2n\rangle}{\mathrm{d}t}=-k_2(\langle(2n)^2\rangle-\langle 2n\rangle) \tag{2}$$

If we set $2n=N$, we have in place of Eq. 2

$$\frac{\mathrm{d}\langle N\rangle}{\mathrm{d}t}=-k_2(\langle N^2\rangle-\langle N\rangle) \tag{2}'$$

Solving this under the initial condition that $N=N_0$ at $t=0$, we obtain

$$\langle N\rangle=\frac{N_0}{1+k_1N_0t+k_2N_0\int_0^t\frac{\sigma^2(t)-\langle N\rangle}{\langle N\rangle^2}\mathrm{d}t} \tag{3}$$

where N_0 is the initial number of reactant molecules and $\sigma^2(t)=\langle N^2\rangle-\langle N^2\rangle$ denotes the variance.

for the initial condition that $N=N_0$ at $t=0$. It should be here noted that Eq. 1, 8 agrees "in the mean" with the result derived by the deterministic theory. If we multiply both sides of Eq. 1, 5 by n^2 and sum over all values of n, we obtain as the differential equation for the second moment $\langle n^2\rangle$

$$\frac{d\langle n^2\rangle}{dt}=-2\frac{k_2N_0}{1+k_2N_0t}\langle n^2\rangle+\frac{k_2N_0}{1+k_2N_0t}\langle n\rangle \tag{1, 9}$$

which is transformed into the form, according to $2n=N$ and Eq. 1, 8,

$$\frac{d\langle N^2\rangle}{dt}+2\frac{k_2N_0}{1+k_2N_0t}\langle N^2\rangle=2k_2\left(\frac{N_0}{1+k_2N_0t}\right)^2 \tag{1, 10}$$

Solving Eq. 1, 10 under the initial condition that $N=N_0$ at $t=0$, we obtain

$$\langle N^2\rangle=\left(\frac{N_0}{1+k_2N_0t}\right)^2+2k_2t\left(\frac{N_0}{1+k_2N_0t}\right)^2 \tag{1, 11}$$

Substituting Eq. 1, 8 into this equation, we have as the variance $\sigma^2(t)=\langle N^2\rangle-\langle N\rangle^2$

$$\sigma^2(t)=2k_2t\langle N\rangle^2 \tag{1, 12}$$

and consequently the coefficient of variation $\bar{\sigma}(t)=\dfrac{\sigma(t)}{\langle N\rangle}$ is expressed in the form

$$\bar{\sigma}(t)=\sqrt{2k_2t} \tag{1, 13}$$

For sufficiently large values of t, the coefficient of variation, which is independent of the initial number of reactant molecules, is considerably large, so that the statistical fluctuation arising inherently in the bimolecular reaction itself may become large compared with the random experimental errors incidental to the observed value $\langle N\rangle$.

Example 2. Lindemann's Mechanism. — Let us consider the collision theory for the unimolecular reaction which is usually associated with the name of Lindemann[10].

$$\begin{array}{ccc} A+A & \rightleftarrows & A^*+A \\ & & \downarrow \\ & & B \end{array}$$

The reaction $A+A\rightarrow A^*+A$ is the activation process by the collision between two inert reactant molecules, the reverse reaction $A+A^*\rightarrow A+A$ is the deactivation process by the collision between an inert reactant molecule and an activated molecule and the spontaneous reaction $A^*\rightarrow B$ is the "true" unimolecular reaction. If we denote by $P(n_a, n_a^*, n_b, t)$ the probability that n_a inert reactant molecules, n_a^* activated molecules and n_b resultant molecules coexist in the reaction system at time t, then we have

$$\begin{aligned}\frac{d}{dt}P(n_a, n_a^*, n_b, t)&=-k^*(t)n_aP(n_a, n_a^*, n_b, t)\\&+k^*(t)(n_a+1)P(n_a+1, n_a^*-1, n_b, t)\\&-k'(t)n_a^*P(n_a, n_a^*, n_b, t)\\&+k'(t)(n_a^*+1)P(n_a-1, n_a^*+1, n_b, t)\\&-kn_a^*P(n_a, n_a^*, n_b, t)\\&+k(n_a^*+1)P(n_a, n_a^*+1, n_b-1, t)\end{aligned} \tag{2, 1}$$

where $k^*(t)$ and $k'(t)$ denote the instantaneous values of the rate constants for the reactions $A+A\rightarrow A^*+A$ and $A+A^*\rightarrow A+A$ respectively and k the rate constant for the true unimolecular reaction $A^*\rightarrow B$. Thus the differential equations for the mean values $\langle n_a\rangle$ and $\langle n_a^*\rangle$ are given by

$$\frac{d\langle n_a\rangle}{dt}=-k^*(t)\langle n_a\rangle+k'(t)\langle n_a^*\rangle \tag{2, 2}$$

and

$$\frac{d\langle n_a^*\rangle}{dt}=k^*(t)\langle n_a\rangle-(k'(t)+k)\langle n_a^*\rangle \tag{2, 3}$$

respectively, which are consistent "in the mean" with Fowler's equations[11].

Multitdimensional Stochastic Model

In comparing the probabilistic theory with the deterministic theory, we have so far considered the one-dimensional stochastic process for the "true" unimolecular gas reaction on the macroscopic point of view. Now consider microscopically the multi-dimensional stochastic process for a reaction system, such that at time t the numbers of reactant molecules in the states of internal energies $\varepsilon_1, \varepsilon_2, \cdots\cdots, \varepsilon_i, \cdots\cdots$ are $n_1, n_2, \cdots\cdots, n_i, \cdots\cdots$, respectively, under the same conditions as in the previous section. Then if we denote the probability for this reaction system by $P(n_1, n_2, \cdots\cdots, n_i, \cdots\cdots, t)=P(\{n_i\}, t)$, we have

10) F. A. Lindemann, *Trans. Faraday. Soc.*, 17, 599 (1921).

11) R. H. Fowler, "Statistical Mechanics", Cambridge University Press (1936), p. 712.

* The internal energy ε_i of reactant molecule changes continually into the enregy ε with various values by the random energy transfer between molecules. Expressing the distribution of such energy ε by $F_i(\varepsilon)$, we have as the averaged specific reaction rate $\langle k_1(\varepsilon_i)\rangle$

$$\langle k_1(\varepsilon_i)\rangle=\int_0^\infty k_1(\varepsilon/\varepsilon_i)dF_i(\varepsilon),$$

where we may take such distribution function that $F_i(0)=0$ and $F_i(\infty)=1$, and $k_1(\varepsilon/\varepsilon_i)=0$ if ε is smaller then the value necessary for a chemical reaction to occur. The k_1 in Eq. 14 denotes such $\langle k_1(\varepsilon_i)\rangle$.

$$\begin{aligned}
&\frac{d}{dt}P(n_1, n_2, \cdots\cdots, n_i, \cdots\cdots, t)\\
&= -k_1^{(1)}n_1P(n_1, n_2, \cdots\cdots, n_i, \cdots\cdots, t)\\
&\quad + k_1^{(1)}(n_1+1)P(n_1+1, n_2, \cdots\cdots, n_i, \cdots\cdots, t)\\
&\quad - k_1^{(2)}n_2P(n_1, n_2, \cdots\cdots, n_i, \cdots\cdots, t)\\
&\quad + k_1^{(2)}(n_2+1)P(n_1, n_2+1, \cdots\cdots, n_i, \cdots\cdots, t)\\
&\quad \vdots\\
&\quad - k_1^{(i)}n_iP(n_1, n_2, \cdots\cdots, n_i, \cdots\cdots, t)\\
&\quad + k_1^{(i)}(n_i+1)P(n_1, n_2, \cdots\cdots, n_i+1, \cdots\cdots, t)\\
&\quad \vdots
\end{aligned} \tag{14}$$

or

$$\begin{aligned}
\frac{d}{dt}P(\{n_i\}, t) = &-\sum_i k_1^{(i)}n_iP(\{n_j\}_{j\neq i}, n_i, t)\\
&+\sum_i k_1^{(i)}(n_i+1)P(\{n_j\}_{j\neq i}, n_i+1, t)
\end{aligned} \tag{14}'$$

where $P(\{n_j\}_{j\neq i}, n_i+1, t) = P(n_1, n_2, \cdots\cdots, n_{i-1}, n_i+1, n_{i+1}, \cdots\cdots, t)$ and the rate constant $k_1^{(i)}$* which is the function of energy ε_i denotes the transition probability that a molecule in the internal state with an energy ε_i is transformed into a resultant molecule during unit time. Let the total number of reactant molecules at time t be $n=\sum_i n_i$ and the initial number of reactant molecules with the internal energy ε_i be n_i^0. If we multiply both sides of Eq. 14 by $\sum_i n_i$ and sum from 0 to n_i^0 $(i=1, 2, \cdots\cdots)$ with respect to each energy state, we obtain

$$\begin{aligned}
\frac{d}{dt}\langle\sum_i n_i\rangle = &-\langle k_1^{(1)}n_1\sum_i n_i\rangle + \langle k_1^{(1)}n_1(\sum_i n_i - 1)\rangle\\
&-\langle k_1^{(2)}n_2\sum_i n_i\rangle + \langle k_1^{(2)}n_2(\sum_i n_i - 1)\rangle\\
&\vdots\\
&-\langle k_1^{(i)}n_i\sum_i n_i\rangle + \langle k_1^{(i)}n_i(\sum_i n_i - 1)\rangle\\
&\vdots\\
= &-\langle\sum_i k_1^{(i)}n_i\rangle
\end{aligned}$$

that is,

$$\frac{d\langle n\rangle}{dt} = -\langle\sum_i k_1^{(i)}n_i\rangle \tag{15}$$

Here if we set

$$\frac{\sum_i k_1^{(i)}n_i}{\sum_i n_i} = \bar{k}_1 \tag{16}$$

Eq. 15 becomes, according to $\sum_i k_1^{(i)}n_i = \bar{k}_1 n$,

$$\frac{d\langle n\rangle}{dt} = -\bar{k}_1\langle n\rangle \tag{17}$$

which formally agrees with Eq. 7. The rate constant $\bar{k}_1$ denotes the "average" probability that one molecule undergoes a chemical transformation during unit time. On comparing Eq. 17 with the conventional rate equation

$$\frac{dn}{dt} = -\bar{k}_1 n, \tag{18}$$

which is statistical only with respect to the rate constant but deterministic with respect to the number of reactant molecules, it should be noticed that the application of the multi-dimensional stochastic model to the "true" unimolecular gas reaction presents us with an excellent method for calculating statistically the rate constant together with the number of reactant molecules.

In order to calculate the variance of the total number of reactant molecules, if we multiply both sides of Eq. 14′ by $(\sum_i n_i)^2$ and sum over all values of each n_i we obtain as the differential equation of the mean value for $(\sum_i n_i)^2$

$$\begin{aligned}
\frac{d}{dt}\langle(\sum_i n_i)^2\rangle = &-2\langle(\sum_i k_1^{(i)}n_i)(\sum_i n_i)\rangle\\
&+\langle\sum_i k_1^{(i)}n_i\rangle
\end{aligned}$$

Using $\sum_i n_i = n$ and $\sum_i k_1^{(i)}n_i = \bar{k}_1 n$, we can transform this to

$$\frac{d\langle n^2\rangle}{dt} = -2\bar{k}_1\langle n^2\rangle + \bar{k}_1\langle n\rangle \tag{19}$$

When we rewrite Eq. 17 by the alternative equation

$$\frac{d\langle n\rangle^2}{dt} = -2\bar{k}_1\langle n\rangle^2 \tag{20}$$

and subtract Eq. 20 from Eq. 19, we obtain, using $\langle n\rangle = n_0\exp(-\bar{k}_1 t)$,

$$\begin{aligned}
&\frac{d}{dt}(\langle n^2\rangle - \langle n\rangle^2) + 2\bar{k}_1(\langle n^2\rangle - \langle n\rangle^2)\\
&\quad = \bar{k}_1 n_0\exp(-\bar{k}_1 t)
\end{aligned} \tag{21}$$

Solving Eq. 21 with respect to the variance $\langle n^2\rangle - \langle n\rangle^2$, we obtain

$$\langle n^2\rangle - \langle n\rangle^2 = n_0\exp(-\bar{k}_1 t)\{1-\exp(-\bar{k}_1 t)\} \tag{22}$$

which agrees with the variance in Bartholomay's macroscopic treatment if we use k_1 in place of $\bar{k}_1$. We observe, however, that $\bar{k}_1$ is estimated by the method to be shown below.

In the reaction system at thermal equilibrium the equilibrium fraction of reactant molecules in the energy state ε_i is given by

$$n_i = n\frac{g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})}{\sum_i g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})} \tag{23}$$

where $g(\varepsilon_i)$ denotes the quantum statistical weight for the state of energy ε_i. Substituting Eq. 23 into Eq. 16, we find

$$\bar{k}_1=\frac{\sum_i k_1^{(i)}(\varepsilon_i)g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})}{\sum_i g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})} \tag{24}$$

If we differentiate logarithmically with respect to T, we obtain

$$kT^2\frac{\partial \ln \bar{k}_1}{\partial T}=\frac{\sum_i \varepsilon_i k_1^{(i)}(\varepsilon_i)g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})}{\sum_i k_1^{(i)}(\varepsilon_i)g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})}$$
$$-\frac{\sum_i \varepsilon_i g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})}{\sum_i g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})} \tag{25}$$

where the first term on the r. h. s. is the average internal energy, not of the existing energized molecules, but of those which react during unit time and the second term is the average internal energy for all molecules[12]. If all reacting molecules that possess energy exceeding ε_0 have the same probability λ_0 for the "true" unimolecular reaction during unit time, then we have the following relations;

$$k_1^{(i)}=0 \quad \text{for} \quad \varepsilon_i<\varepsilon_0,$$
$$k_1^{(i)}=\lambda_0 \quad \text{for} \quad \varepsilon_i\geqq\varepsilon_0.$$

Eq. 24 is therefore transformed into

$$\bar{k}_1=\frac{\lambda_0\sum_{\varepsilon_i\geq\varepsilon_0} g(\varepsilon_i)\exp(\varepsilon_i/\boldsymbol{kT})}{\sum_i g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})} \tag{26}$$

If we treat the internal vibration of molecule as consisting of linear harmonic oscillators whose energy levels are continuous, we have $g(\varepsilon)\propto\varepsilon^{s-1}\Delta\varepsilon$ within a certain range of $\Delta\varepsilon$ and can approximate the r. h. s. of Eq. 26 by the distribution function of I'-type

$$\frac{\lambda_0}{I'(s)}\int_{\varepsilon_0}^{\infty}\left(\frac{\varepsilon}{\boldsymbol{kT}}\right)^{s-1}\exp(-\varepsilon/kT)\frac{d\varepsilon}{\boldsymbol{kT}}$$

where $I'(s)=(s-1)!$. Hence we have in place of Eq. 26

$$\bar{k}_1\simeq\lambda_0\exp(-\xi_0/\boldsymbol{kT})\sum_{r=0}^{s-1}\frac{1}{r!}\left(\frac{\varepsilon_0}{\boldsymbol{kT}}\right)^r \tag{27}$$

where ε_0 denotes the minimum energy required for reaction. But if $\varepsilon_0\gg s\boldsymbol{kT}$, the overall rate constant $\bar{k}_1$ is approximately given by

$$\bar{k}_1\simeq\frac{\lambda_0}{I'(s)}\left(\frac{\varepsilon_0}{\boldsymbol{kT}}\right)^{s-1}\exp(-\varepsilon_0/\boldsymbol{kT}) \tag{27}'$$

And more generally, if we denote the probability for the distribution of higher energy levels than ε_0 by $g(\varepsilon_i-\varepsilon_0)/g(\varepsilon_i)$, $k_1^{(i)}$, the specific reaction rate for molecules of energy $\varepsilon_i\geqq\varepsilon_0$, is proportional to this probability. We then have the relations

$$k_1^{(i)}=0 \quad \text{for} \quad \varepsilon_i<\varepsilon_0$$
$$k_1^{(i)}=Ag(\varepsilon_i-\varepsilon_0)/g(\varepsilon_i) \quad \text{for} \quad \varepsilon_i\geqq\varepsilon \tag{28}$$

where A is the proportional coefficient and we define $g(\varepsilon_i-\varepsilon_0)=0$ for $\varepsilon_i\leqq\varepsilon_0$. Thus substituting Eq. 28 into Eq. 24, we obtain

$$\bar{k}_1=A\exp(-\varepsilon_0/\boldsymbol{kT})$$
$$\times\frac{\sum_{\varepsilon_i\geq\varepsilon_0} g(\varepsilon_i-\varepsilon_0)\exp\{-(\varepsilon_i-\varepsilon_0)\boldsymbol{kT}\}}{\sum_i g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})}$$
$$=A\exp(-\varepsilon_0/\boldsymbol{kT})\frac{\sum_{\varepsilon_i'} g(\varepsilon_i')\exp(-\varepsilon_i'/\boldsymbol{kT})}{\sum_i g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})}$$

where $\varepsilon_i'=\varepsilon_i-\varepsilon_0$. If, however, we use the same model molecule composed of a set of simple harmonic oscillators of equal frequency as in Kassel's theory[13], $\sum_{\varepsilon_i'} g(\varepsilon_i')\exp(-\varepsilon_i'/\boldsymbol{kT})$ is equal to $\sum_i g(\varepsilon_i)\exp(-\varepsilon_i/\boldsymbol{kT})$, and consequently we obtain the Arrhenius' equation

$$\bar{k}_1=A\exp(-\varepsilon_0/\boldsymbol{kT}) \tag{29}$$

And from Eqs. 28 and 29 $k_1^{(i)}$ is given by

$$k_1^{(i)}=\bar{k}_1\exp(-\varepsilon_0/\boldsymbol{kT})\frac{g(\varepsilon_i-\varepsilon_0)}{g(\varepsilon_i)} \tag{30}$$

where $\varepsilon_i\geqq\varepsilon_0$.

Conclusions

We have clarified the probabilistic foundations for the application of the theory of the stochastic process to the "true" unimolecular reaction. By extending Bartholomay's method to the more general stochastic process having the parameter $k(t)$ variable with time, we have shown that the theory of stochastic process can be applied to any chemical reaction other than the unimolecular reaction. We have also noticed that the averaged rate constant $\bar{k}_1$ of the "true" unimolecular reaction is legitimately calculated by the application of the multidimensional stochastic process to the chemical reaction.

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12) R. H. Fowler and E. A. Guggenheim, Ref. 5, p. 522.

13) L. Kassel, *J. Phys. Chem.*, 32, 225, 1065 (1928).

The Functional Groups of Sachaconitine

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In a previous paper[1] the extended formula of sachaconitine (I) ($C_{23}H_{37}O_4N$), one of the alkaloids of *Aconitium miyabei* Nakai, was given as follows:

$$C_{19}H_{24}\begin{cases}(OH)_2\\(OCH_3)_2\\N\text{-}C_2H_5\end{cases}$$

Experiments for characterizing the functional groups of "compound I" have been carried out, and the results are here comunicated.

Oxidation of "compound I" with potassium permanganate in acetone gave a mixture of (a) a neutral compound (II), m. p. 194~196°C, $[\alpha]_D$ −37.8 (EtOH) (Found: C, 67.92; H, 8.71; N, 3.51. Calcd. for $C_{23}H_{35}O_5N$: C, 68.12; H, 8.70; N, 3.45%), and (b) a basic compound (III), m. p. 230~231°C, $[\alpha]_D$ +17.1° (EtOH), pK_a 9.8, ν_{max} 3545, 3447 cm^{-1} (OH), 3230 cm^{-1} (NH) (Found: C, 69.30; H, 8.97; N, 4.04. Calcd. for $C_{21}H_{33}O_4N$: C, 69.39; H, 9.15; N, 3.85%).

"Compound II" was characterized as the lactam, oxosachaconitine, by its infrared spectrum, ν_{max} 3537, 3447 cm^{-1} (OH), 1635 cm^{-1} (lactam), and by treatment with lithium aluminum hydride, which converted it into "compound I".

"Base III" was shown to be *N*-desethylsachaconitine by treatment with ethyl iodide, which also reverted to "compound I", thus firmly establishing the presence of an *N*-ethyl group in the alkaloid. Treatment of "compound II" with acetylchloride gave diacetyloxosachaconitine, m. p. 149~151°C, ν_{max} 1725 cm^{-1} (ester carbonyl), 1625 cm^{-1} (lactam) (Found: C, 64.15; H, 8.00; N, 3.01. Calcd. for $C_{27}H_{39}O_7N$: C, 64.49; H, 8.44; N, 3.01%). On the same treatment, "compound III" gave a neutral product in very poor yield, which could not be purified. Hence "compound III" was treated with acetic anhydride in pyridine at room temperature, and then a neutral product, m. p. 175~176°C, was yielded. In the infrared spectrum this product showed an amide band at 1635 cm^{-1}, hydroxyl bands at 3487 and 3331 cm^{-1}, but no ester carbonyl band. With the same reagent "compound I" or "II" were recovered without change, and thus it was suggested that the hydroxyls of the alkaloid resisted acetylation with acetic anhydride at room temperature. Oxidation of "compound I" with chromic acid—pyridine complex or with potassium permanganate in acetone-acetic acid produced again two products: one was a neutral compound (IV), m. p. 237~239°C, $[\alpha]_D$ +35.7° (EtOH), λ_{max} 290 mμ (ε 40) (Found: C, 68.46; H, 8.25; N, 3.62. Calcd. for $C_{23}H_{35}O_5N$: C, 68.46; H, 8.24; N, 3.47%), the second was a base (V), m. p. 275~277°C, $[\alpha]_D$ +107° (EtOH), pK_a 8.3 (Found: C, 70.35; H, 8.00; N, 4.04. Calcd. for $C_{21}H_{29}O_4N$: C, 70.17; N, 8.13; N, 3.90%). "Compound IV", also obtainable from "compound II" by oxidation with chromic acid in acetone, showed a hydroxyl band at 3470 cm^{-1} a lactam band at 1619 cm^{-1} and a five-membered carbonyl band at 1745 cm^{-1} in infrared. Reduction of "compound IV" with sodium borohydride produced "compound II", and with lithium aluminium hydride gave back "compound I". Thus "compound IV" is a keto-lactam, oxosachaconitinone, and also it is indicated, that one of the two hydroxyls in "compound I" or "II" is a secondary one in a five-membered ring.

"Base V" showed a band at 1741 cm^{-1} due to the five-membered ketone carbonyl, a band at 3300 cm^{-1} and no double bond band in infrared, and in ultraviolet spectrum this base contained two maxima at 290 mμ (ε 70) and 250mμ (ε 210) due to ketone carbonyl respectively. Confirmation of base V as a *N*-desethyl base was supported by the facts that the base gave "compound III" on reduction with sodium borohydride and was obtained also from "compound III" by oxidation with chromic acid in acetone; accordingly the above noted band at 3300 cm^{-1} may be due to N-H group. Thus the results of ultraviolet and infrared absorptions give the assumption, that in "base V" two hydroxyls of "compound III" were oxidized to diketo groups both being five-membered cyclic ketones without more free hydroxyl present.

This consideration was further tested by treatment of "base V" with acetic anhydride in pyridine at room temperature, which as above mentioned, is not capable of acetylating the hydroxyls of the alkaloid. The neutral product obtained, m. p. 222~224°C, showed

1) H. Suginome, N. Katsui and G. Hasegawa, This Bulletin 32, 604 (1959).

a band at 1755 cm^{-1} (carbonyl) and 1616 cm^{-1} (amide), but no hydroxyl band in infrared. On the other hand, one maximum (290 mμ, ε 70) in ultraviolet of "base V" is normal and may be caused by the same carbonyl as that of "compound IV", but the second (250 mμ, ε 210) is abnormal. The same abnormality in ultraviolet has been already shown in dehydrodelpheline[2] (250 mμ, ε 200), obtainable by oxidation of the delphinium alkaloid, delpheline, having the same skeletal formula ($C_{21}H_{33}N$) as sachaconitine.

Furthermore the decrease of pK_a in the conversion from "compound I" (pK_a 9.7) or "compound III" (pK_a 9.8) to "compound V" (pK_a 8.3) has been also observed analogously in the change of parent alkaloid to a dehydroderivative. Then it may be assumed, that in "compound V" a carbonyl is present at the analogous position with dehydrodelpheline. Thus "compound V" is assigned the name, *N*-desethyldehydrosachaconitinone; the environment of the ring containing nitrogen in "compound I" is considered to resemble that of delcosine[3], one of the delphinum alkaloids, because the *N*-ethyl group of the former is more readily oxidized as well as the latter to a *N*-desethyl derivative than the other delphinum or aconitum alkaloids.

But it may be more plausible to assume, that the position of a carbonyl in "compound V" is not the same with didehydrodelcosine[4] but with dehydrodelpheline[5], since the carbonyl is a five-membered ring ketone.

Investigation concerning the methoxyl functions of the alkaloid is in progress and will be reported later.

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2) R. C. Cookson and M. E. Trevett, *Chem. and Ind.*, 1324 (1954), *J. Chem. Soc.*, **1956**, 2689.
3) R. Anet, D. W. Clayton and L. Marion, *Can. J. Chem.*, **35**, 397 (1957).
4) V. Skaric and L. Marion, *J. Am. Chem. Soc.*, **80**, 4434 (1958).
5) R. C. Cookson and M. E. Trevett, *J. Chem. Soc.*, **1956**, 3121.

Inorganic Extraction Studies on the System between Bis(2-ethyl hexyl)-orthophosphoric Acid and Hydrochloric Acid (I)

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During the last decade, alkyl esters of orthophosphoric acid as liquid-liquid solvent extraction reagents have been investigated widely for both chemical and chemical engineering purposes. A number of review articles on this subject[1,2] have been published. Among the esters, tributyl phosphate is beneficially used in several processes of the recovery of uranium and plutonium as well as in many other chemical separation techniques.

Bis(2-ethyl hexyl)-orthophosphoric acid, commonly abbreviated as HDEHP or D2EHPA, has been employed as a liquid-liquid extraction reagent primarily for uranium by Blake et al.[3] at Oak Ridge National Laboratory, and furthermore by Peppard et al. for berkelium-(IV)[4] and lanthanides[5]. Some physicochemical studies have also been performed by Peppard[6,7], Baes and others[8]. Recently, some metal complexes of this reagent were prepared by Peppard and Ferraro[9] and their infrared spectra were also surveyed.

However, no comprehensive study on the

1) C. A. Blake, Jr., C. F. Baes, Jr., K. B. Brown, C. F. Coleman and J. C. White, "Proceeding of the Second International Conference on the Peaceful Uses of Atomic Energy", A/Conf. 15/P/1550 (1958).
2) G. H. Morrison and H. Freiser, "Solvent Extraction in Analytical Chemistry", John Wiley & Sons. Inc., New York (1957), p. 146.
3) C. A. Blake, D. J. Crouse, C. E. Coleman, K. B. Brown and A. D. Klemers, USAEC ORNL-2172 (1956).
4) D. F. Peppard, S. W. Moline and G. W. Mason, *J. Inorg. Nucl. Chem.*, **4**, 344 (1957).
5) D. F. Peppard, G. W. Mason and S. W. Moline, ibid., **5**, 141 (1957).
6) D. F. Peppard, G. W. Mason, W. J. Driscoll and R. J. Sironen, ibid., **7**, 276 (1958).
7) D. F. Peppard, G. W. Mason, J. L. Maier and W. J. Driscoll, ibid., **4**, 334 (1957).
8) C. F. Baes, Jr., R. A. Zingaro and C. F. Coleman, *J. Phys. Chem.*, **62**, 129 (1958).
9) D. F. Peppard and J. R. Ferraro, *J. Inorg. Nucl. Chem.*, **10**, 275 (1959).

extraction from a given mineral acid solution has been reported. In the present paper, the influence of acid concentration is presented and discussed when the extraction is carried out from hydrochloric acid solution containing each of about fifty elements.

Experimental

Solvent.—The bis(2-ethyl hexyl)-orthophosphoric acid received from Virginia Chemicals, Co. was purified according to the method of Peppard[7,10]. All treatments were manually performed using two separatory funnels. The purity of the solvent was checked by the determination of the distribution ratio, K_d, for lanthanum and iron[1,6]. The work reported here was carried out using HDEHP diluted to 50 volume percent with toluene of chemically pure grade.

Determination of Distribution Ratios.—The distribution ratio, K_d, of a given nuclide (or nuclides), defined as the concentration of nuclide in the organic layer divided by that in the aqueous layer, was determined radiometrically. In the determination, a portion of an aqueous acid solution of a given concentration containing the radioactive tracer was shaken with a portion of the solvent which had been previously equilibrated with the corresponding barren aqueous acid.

Details of the method of the determination were as follows. Two millilitres each of aqueous acid and pre-equilibrated HDEHP were placed in a 5 ml. glass-stoppered measuring-cylinder, and shaken vigorously. After the two layers were transferred together into a centrifuge tube, the content was centrifuged at 4000 rpm for 1 min. Nearly all of the aqueous layer was transferred with a transfer pipette to a new centrifuge tube. Both tubes were centrifuged for 1 min. again. Aliquots of each layer were taken into two glass-stoppered tubes for the radioassay. The quantity of the aliquots taken was usually 1 ml.

In several cases, a portion of the organic extract obtained was transferred to a new 5-ml. cylinder, shaken with an equal volume of fresh aqueous acid, and treated again as mentioned above. Further scrubbings were made in a few cases. By these scrubbings and the following redetermination of K_d values, difficulties caused by the undesired metal hydrates were obviated.

The greater part of the data was obtained by γ-ray scintillation counting. The counter was a Philips Model PW 4022-52-32 counting unit and the scintillator was a well-type Na(Tl)I crystal "7F8" made by Harshow Chemicals Co. In cases of β- and α-ray emitters aliquot portions from both layers were carefully dried up on small stainless steel or platinum disks, under an infrared lamp or in an induction furnace avoiding any loss of activity and dissolution of stainless steel in hydrochloric acid. β-Counting was performed with a G-M counter having a mica window of 2.1 mg./cm^2 thick made by Rikagaku Kenkyujo, and α-rays with a proportional counter of Nuclear Measurement Corp. or with an α-ray scintillation counter of Nihon-Musen Irigaku Kenkyujo.

Remarks on the Determination.—Almost all data in this experiment were obtained after shaking the two layers for two minutes. According to Peppard and his co-workers[7], the equilibrium of extraction of ^{147}Pm was attainable in a mixing period of less than 30 sec. Thus the equilibrium might be attained within two minutes for almost all elements. The K_d values for magnesium, aluminum, titanium, vanadium and silver were obtained by one minute shaking, because their half-lives are short.

The range of acidity of the aqueous hydrochloric acid solution covered mainly from 0.01 to 2 N. In some cases, it was extended to 12 N. The acidity was determined volumetrically, when necessary. Although the amount of the elements in the initial 2 ml. of the hydrochloric acid solutions was made as small as possible, it varied from tracer amount to about 1 mg. Details are shown in Table I. In all cases, the specific activity was higher than 10^4 cpm/mg. under a given condition of measurement.

All experiments were carried out at 21 ± 3°C. Within this range, the variations in K_d values have been shown to be within experimental error.

Radioisotopes Used.—The radioactive isotopes used in this experiment were mainly prepared by irradiation of high purity targets in a water-boiler type reactor (Japan Research Reactor I, (neutron flux: 5×10^{11} n/sec. cm^2), whereas some of the isotopes were imported from Oak Ridge National Laboratory, U.S.A. or Radiochemical Centre, U.K.

The radiochemical purity of the isotopes was checked by their half-lives, γ-ray spectra, and/or β-ray absorption curves with aluminum foils. The γ-ray spectrograms were obtained with an RCL 256 channel γ-ray spectrometer or a single channel spectrometer made by Tokyo Shibaura Denki Co.

Table I[14-21] shows the radio-isotopes used[11], together with their half-lives and mass numbers, the target materials or sources, the method of checking the radiochemical purity, and the weight of the materials added in the initial 2 ml. of hydrochloric acid solutions.

Usually the irradiated targets were dissolved in hydrochloric acid and used without further treatment. For example, lanthanum oxide, magnesium

10) D. C. Stewart and H. W. Crandall, *J. Am. Chem. Soc.*, 73, 1377 (1951).

11) K. Kimura, "Hoshasen Data Book", Chijin Shokan, Tokyo (1958), p. 92.

12) N. Shibata and K. Yoshihara, This Bulletin, 32, 422 (1959).

13) H. Ebihara and K. Yoshihara, ibid., in press.

14) K. A. Kraus and F. Nelson," Proceeding of the International Conference on the Peaceful Uses of Atomic Energy", Geneva, A/Conf. 8/p/837 (1955); Vol. VII, United Nations Publication, New York (1956), p. 118.

15) Green and Kafalas, *J. Chem. Phys.*, 22, 760 (1954).

16) T. Ishimori, E. Nakamura and K. Watanabe, This Bulletin, in press.

17) T. Nakai and S. Yajima, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, 79, 1267 (1958).

18) T. Ishimori, H. Umezawa and K. Watanabe, *J. Atomic Energy Soc. Japan*, 1, 299 (1959).

19) S. Yajima, This Bulletin, 31, 699 (1958).

20) K. A. Kraus and G. E. Moore, *J. Chem. Soc.*, 72, 4293 (1950).

21) C. J. Rodden, editor in chief, "Analytical Chemistry of the Manhattan Project", McGraw Hill, New York (1950), p. 83.

TABLE I. RADIOISOTOPES USED

Nuclide	Target material or source	Radiochemical purity was checked by	Weight	Remarks
15.0 hr. Na-24	$NaNO_3$, G. R.	γ-spec., γ-decay	100 γ	
9.45 min. Mg-27	Mg metal, 99.99%	γ-decay	250 γ	
2.27 min. Al-28	Al metal, 99.99%	γ-decay, γ-spec.	250 γ	
37.3 min. Cl-38	NH_4Cl, G. R.	γ-decay	250 γ	
12.51 hr. K-42	KNO_3, G. R.	γ-spec., γ-decay	100 γ	
164 d. Ca-45	imported		60 γ	$CaCl_2$ in HCl soln.
85 d. Sc-46	imported		60 γ	$ScOl_3$ in HCl soln.
5.80 min. Ti	Ti-hydroxide	γ-decay	250 γ	
3.76 min. V-52	NH_4VO_3, G. R.	γ-decay	5 γ	
27.8 d. Cr-51	Cr-dye, R. I.		~tracer	
2.58 hr. Mn-58	MnO_2, G. R.	γ-decay	250 γ	
3.0 y. Fe-55	imported		10 γ	
45.1 d. Fe-59				$FeCl_3$ in HCl soln.
5.2 y. Co-60	imported			$CoCl_2$ in HCl soln.
2.56 hr. Ni-65	Ni metal	γ-decay	0.5 mg.	Co-58 was removed by ion exchange[14].
12.8 hr. Cu-64	Cu metal, 99.9%	γ-decay	100 γ	
245 d. Zn-65	imported		5 γ	$ZnCl_2$ in HCl soln.
14.2 hr. Ga-72	Ga_2O_3, J. M.	γ-spec., γ-decay	100 γ	
11.4 d. Ge-71	Ge metal, 99.9%	γ-decay	500 γ	Separated from As-77 by benzene extraction[15].
26.5 hr. As-76	As_2O_3, G. R.	γ-decay	500 γ	
127 d. Se-75	Se metal, G. R.	γ-decay, γ-spec.	300 γ	
4.5 hr. Br-80 m	NH_4Br, G. R.	γ-decay	250 γ	
35.9 hr. Br-82				
19 d. Rb-86.	RbCl, G. R.	γ-decay	1 mg.	Cooled for five hours.
28 y. Sr-90	imported		tracer	$SrCl_2$ in HCl soln.
64 hr. Y-90	imported Sr-90	β-abs., β-decay	tracer	
65 d. Zr-95	imported		tracer	Oxalate, β-activity of Nb-95 was eliminated with a 17.6 mg./cm^2 Al absorber.
17.0 hr. Zr-97	UO_2-Oxalic acid	γ-spec.	tracer	Separated by method 17) and 18). Counted at 0.65~0.8 MeV.
35 d. Nb-95	imported Zr-95	β-decay, β-abs.		Oxalate ; separated by Yajima's method[19].
67 hr. Mo-99	$(NH_4)MoO_4$, G. R.	γ-spec., β-decay		
2.12×10^5 y. Tc-99	imported		tracer	Sodium pertechnetate in KOH soln.
1.0 y. Ru-106	imported			$RuCl_3$ in HCl soln.
17 d. Pd-103	Pd metal, J. M.	γ-decay	250 γ	
13.6 d. Pd-109				
2.3 min. Ag-108	Ag metal, 99.9%	γ-decay	50 γ	
53 hr. Cd-115	Cd metal, J. M.	γ-spec.	210 γ	
43 d. Cd-115 m				
54.0 min. In-116 m	$In(OH)_3$, R. I.	γ-spec, β-decay	100 γ	
112 d. Sn-113	Sn metal, 99.997%	γ-spec.	750 γ	
2.75 d. Sb-122	Sb metal, 99.99%	γ-decay	750 γ	
33.5 d. Te-129 m, etc.	Te metal, G. R.		1 mg.	
8.06 d. I-131	imported		tracer	
30 y. Cs-137	imported		tracer	CsCl in HCl soln.
85 min. Ba-139	$BaCO_3$, J. M.	γ-decay	50 γ	
40.2 hr. La-140	La_2O_3, J. M.	γ-decay	100 γ	
46 d. Hf-181	imported		~tracer	$HfOCl_2$ in HCl soln.
111 d. Ta-182	imported			Potassium tantalate in KOH soln

TABLE I (Continued)

23.9 hr. W-187	W oxinate, R. I.	γ-decay	~tracer	
3.87 d. Re-186 17 hr. Re-188	Re metal, J. M.	γ-decay	500 γ	
15 d. Os-191 31 hr. Os-193	Os metal, J. M. or imported Os-191	γ-decay	250 γ	Na_2CO_3-$NaNO_3$ fusion Osmate in NaOH soln.
74.4 d. Ir-192 19 hr. Ir-194	Ir metal, J. M.	γ-decay	50 γ	Na_2O_2 fusion.
4.5 d. Pt-193 18 hr. Pt-197	Pt metal, 99.9%	β, γ-decay	50 γ	
2.69 d. Au-198	Au metal, 99.9%	γ-decay	10 γ	
48 d. Hg-203	imported		5 γ	$Hg(NO_3)_2$ in HNO_3 soln.
4.0 y. Tl-204	imported		tracer	
3.64 d. Ra-224	imported Th-228	α-decay	tracer	Separated by TBP extraction[16].
24.1 d. Th-234	uranyl chloride	γ-spec. γ-decay	tracer	Separated by TBP extraction[16].
27.4 d. Pa-233	ThO_2	γ-spec. γ-decay	tracer	Separated by ion exchange[20].

G. R.: Guaranteed reagent.
J. M.: "Spec-pure" standard source produced by Johnson-Matthey Chemicals Co.
R. I.: High purity target produced by the Radioisotope Production Group, JAERI.

metal, sodium nitrate and barium carbonate were simply dissolved in hydrochloric acid after irradiation. Some of the irradiated targets were dissolved in nitric acid, aqua regia or sodium hydroxide solution and converted into hydrochloric acid solution. For example, rhenium and silver were primarily dissolved in nitric acid, platinum and gold in aqua regia, and arsenous oxide was dissolved in sodium hydroxide solution.

It is likely that the K_d values for arsenic were not largely affected by sodium chloride resulting from sodium hydroxide, for only one drop of tracer solution was added into 2 ml. of the aqueous phase.

Chromium and tungsten tracers were prepared by Yoshihara and Ebihara[12,13], Radioisotope Production Group, Japan Atomic Energy Research Institute. Both were of a high specific activity. On the other hand, most of the imported tracers were used as received.

Some special precautions taken both for the preparation of tracers and for the measurement of distribution ratios are given below in detail:

Vanadium.—Irradiated ammonium metavanadate was dissolved in hot 5 N hydrochloric acid and used without any further treatment. Hence, the chemical form of the vanadium tracer was not clearly known. It might have remained in the V(V) state. *Selenium.*—Irradiated selenium was dissolved in nitric acid containing bromine water, and then converted into a hydrochloric acid solution. The resultant solution was used without heating, as selenic tracer, whereas selenous tracer was obtained by heating the solution in 3 N hydrochloric acid. *Molybdenum.*—Irradiated ammonium molybdate showed a pale purple tint, and the hydrochloric acid solution colored blue-green. It was likely that this color came from a certain reduced chemical form. However, the solution was used without any further treatment, e. g., oxidation. *Antimony.*—Irradiated antimony was dissolved in hydrochloric acid containing a small volume of nitric acid. In an acid range below 2 N, obvious hydrolysis occurred. As the K_d values for 3 N acid is fairly high, being as high as 0.2, the HDEHP solution of antimony that had been prepared by extracting antimony(III) from 3 N hydrochloric acid solution was used as the organic phase. *Tantalum.*—Tantalum-182 solution was acidified with hydrochloric acid, and hydrated tantalum precipitate was centrifuged off. The supernatant solution was used as the tracer solution. *Iridium.*—Fusion with sodium peroxide was more rapid and complete than sodium nitrate-carbonate fusion. *Mercury.*—A dilute nitric acid solution of imported mercury tracer was dropped into hydrochloric acid of known concentration, and used without any further treatment. Both phases were clear after the contact. *Thallium.*—Thallic chloride solution was prepared by oxidation of Tl(I) solution with ceric ammonium nitrate or potassium bromate. *Uranium.*—K_d values for uranium were obtained photometrically[21].

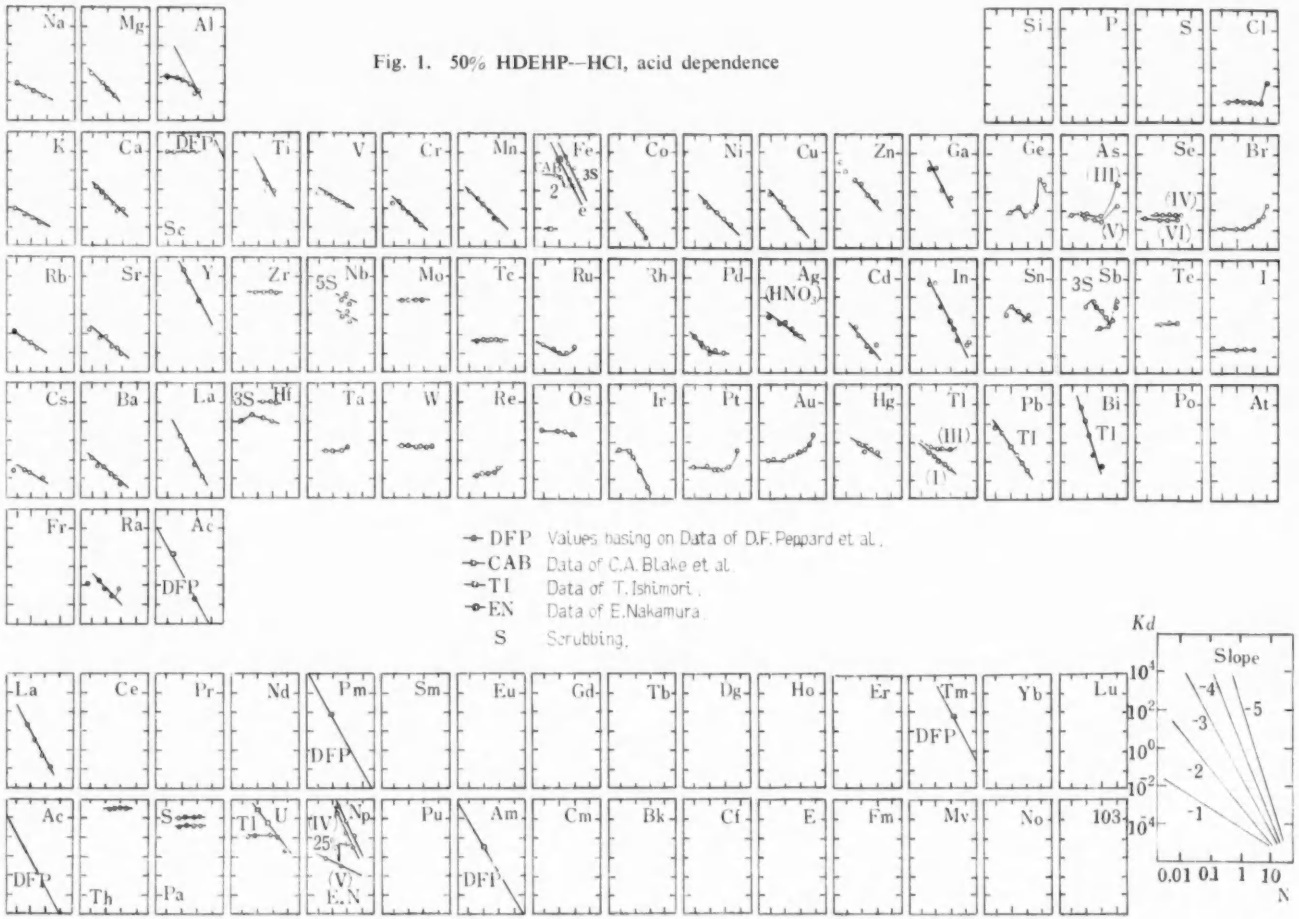
Results and Discussion

The results are summarized in Fig. 1 as a series of graphs of $\log K_d$ vs. $\log N$, where K_d is the distribution ratio and N the acidity in normality. Fig. 1 was compiled from some published and unpublished results. Data for lead, bismuth and americium were taken from the observation of Ishimori[22]. Data for neptunium were taken from the work of Nakamura[23].

Peppard and his coworkers reported that the K_d values for selected lanthanide and actinide cations (III) in the system of HDEHP—perchloric acid are inverse third power dependent on the hydrogen ion concentration in the aqueous phase (0.15 M HDEHP—toluene solution) and direct third power dependent on

22) T. Ishimori, unpublished.
23) E. Nakamura, unpublished.

Fig. 1. 50% HDEHP—HCl, acid dependence



the solvent concentration. The results for yttrium and lanthanum of the present author agree with those of Peppard in K_d values. Therefore, K_d values for thulium, promethium, actinium and americium were taken from their data corrected for 50% HDEHP (1.5 M) assuming that the solvent dependence remains unchanged at this high concentration.

According to Peppard and his coworkers[6,9] and Baes et al.[8], the K_d values for scandium, thorium and uranium for diluted HDEHP solution are inverse third, fourth and second power dependent on the hydrogen ion concentration in the aqueous phase, respectively. However, the concentration of HDEHP is so high in this experiment that the K_d values for these elements show almost horizontal curves. It is caused by the limitation of the method of determination. The fact that the horizontal K_d curve for uranium is lower than those for thorium and scandium is mainly brought about by the difference in the method of K_d determinations. The same can be said for protactinium, zirconium and hafnium, whereas the fourth power acid dependence of K_d values is obtained for titanium. Ishimori's data for uranium in the system of 0.75 M HDEHP solution and hydrochloric acid solution are also added after correction for the concentration of HDEHP. The K_d values show inverse second power dependence on the hydrogen ion concentration in the aqueous phase.

As Fig. 1 shows, the shape of the curves is roughly divided into two types. The first type consists of those in which the absolute figures of the slope are identical with the ionic charges or at least the figures are below minus one. On the other hand, the K_d values of the second type are unaffected by the hydrogen ion concentration in the aqueous phase in the acid range below about 2 N.

The K_d values for alkali metals, alkaline earth metals and lanthanide elements are characteristic of the first type, showing first, second and third power dependence on the hydrogen ion concentration in the aqueous phase, respectively. A similar relationship holds for the elements of Ib, IIb and IIIb group in the periodic table except in the case of gold.

The extraction of metal cation with HDEHP is expressed generally in the following equation[1,9]:

$$M^{m+}{}_{(aq)} + m(HDEHP)_{2\,(org)} \rightleftarrows MH_m(DEHP)_{2m\,(org)} + mH^+{}_{(aq.)}$$

$$K_d = K \cdot [(HDEHP)_{2\,(org)}]^m \cdot [H^+{}_{(aq)}]^{-m} \qquad (1)$$

where, K is the constant of the above equilibrium. In this equation, $(HDEHP)_{2\,(org)}$ represents the dimer of HDEHP in the organic phase[24]. Eq. 1 indicates that an ion with $+m$ charge shows a curve of $-m$ slope. It appears as if an element giving a K_d curve of the first type behaves as a cation in the given system.

On the other hand, the K_d curves for chlorine, bromine and iodine are typical of the second type. Germanium, arsenic, platinum and gold give curves of a similar shape. Almost all of these elements give higher K_d values in an acid solution over 2 N than in 1 N. It is likely that the extraction of these elements is not based on the chelation mentioned above, but on partition, as is found in the case of extraction with TBP[25].

Although the three light elements of Va, VIa and VIIa group, vanadium, chromium and manganese, show the characteristic curves of the first type, the heavy elements of the groups, niobium, molybdenum, technetium, tantalum, tungsten and rhenium, show those of the second type. This appears to be in accord with the fact that Cr(III) and Mn(II) are apt to behave in cationic state in hydrochloric acid media, whilst niobium, molybdenum, technetium, tantalum, tangsten and rhenium are not. The present K_d values for vanadium were relatively low. Vanadinyl(IV) ion in the system HDEHP-sulfate solution, however, shows high K_d values which depend on the hydrogen ion concentration with a slope of ca. -2[1].

Chromium resembles manganese more than it does molybdenum or tungsten as regards the type of acid concentration-K_d value relation. Besides, the slope of ca. -2 for chromium gives a suggestion that chromium exists as a mixture of hydrated chloro-complexes. K_d values for molybdenum and niobium are relatively high, while those for technetium and rhenium are very low.

In contrast with the Va, VIa and VIIa groups, the light elements of IVb, Vb and VIb group, germanium, arsenic and selenium, show K_d curves of the second type, while heavy elements, lead and bismuth, show that of the first type.

It is known that iron(III) and aluminum require a long time to attain extraction equilibrium[1]. In graph "Fe" in Fig. 1, curve 2 shows K_d values for 2 min. shaking, line 3s those for three times scrubbing, line e those for thirty hours shaking. Line e has a slope of -3. In all three cases, iron gives high K_d values, while cobalt and nickel give low values throughout the acidity range. For aluminum,

24) D. F. Peppard, J. R. Ferraro and G. W. Mason, *J. Inorg. Nucl. Chem.*, 4, 371 (1957).
25) D. Dyrssen and F. Krasovec, *Acta Chem. Scand.*, 13, 568 (1959).

the K_d values for the equilibrium were not obtained, because the aluminum tracer used was short-lived.

It is difficult to account for the difference in the behavior of the platinum elements because the methods used in preparing the tracers were quite different. The K_d values for osmium are relatively high, those for iridium show -4th power acid dependence, and those for others are low.

Indium gives a straight line of slope ca. -3 over the acidity range from 0.05 to 10 N. Copper, silver, zinc, cadmium and gallium also behave similarly giving the slope of $-m$. It is generally accepted that these elements form chloro-complexes easily. However, the absolute figures of the slopes for these are nearly equal to those of ionic charges in such condition that the elements do not form chloro-complexes.

As was mentioned by Peppard and his coworkers[6], Eq. 1 is principally analogous to that of the equilibrium found for the extraction of metals with thenoyl trifluoroacetone, HTTA. Figs. 2 and 3 show the comparison between HDEHP and HTTA extraction for

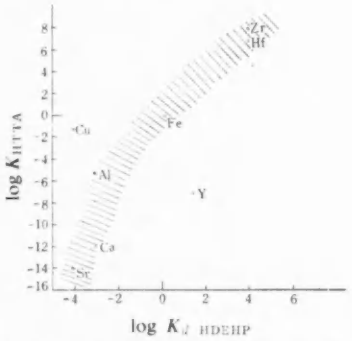


Fig. 2. Relation between $K_{d\ HDEHP}$ and K_{HTTA} values.

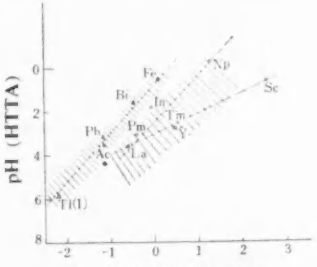


Fig. 3. Relation between $\log N_{1/2}$ for HDEHP system and $pH_{1/2}$ for HTTA system.
○ 0.5 M HTTA ; △ 0.25 M HTTA

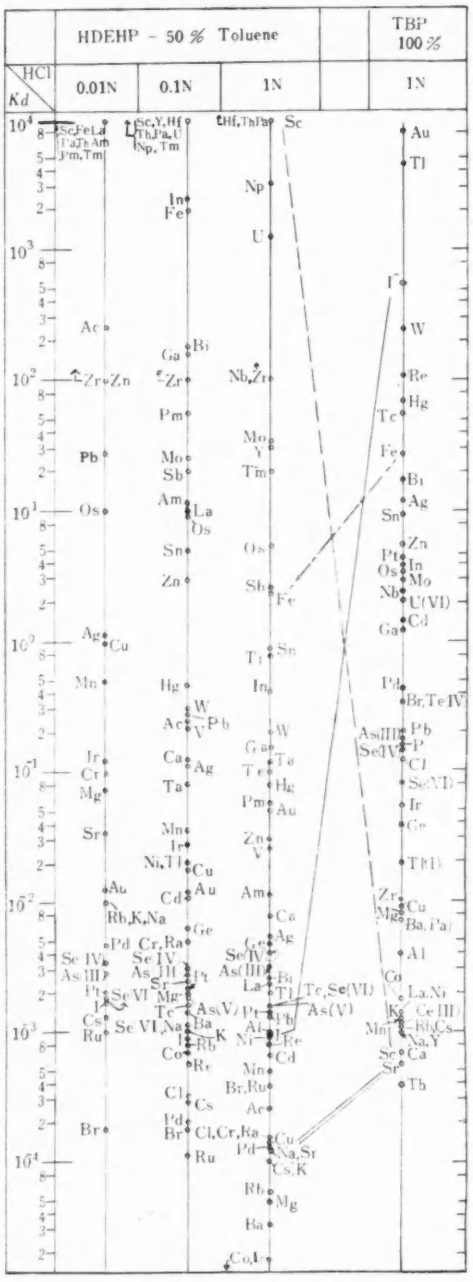


Fig. 4. K_d values in 50% HDEHP—0.01 ~1 N HCl and comparison with 100% TBP—1 N HCl.

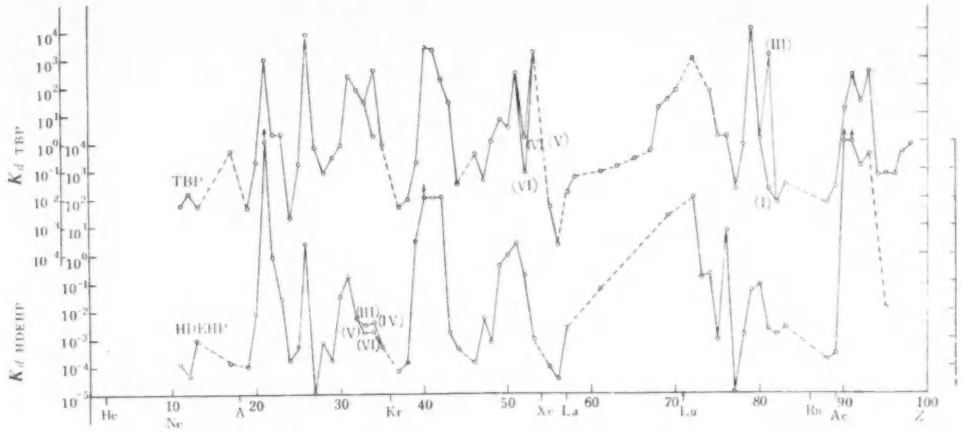


Fig. 5. Relation between K_d values and Z.

some cations. The K_d values for 50% HDEHP at 1 N hydrochloric acid are plotted against K_{HTTA} values*[26,27]. In Fig. 3, the acidity given by $\log K_d = 0$ with HDEHP are plotted against the pH values giving 50% extraction with HTTA[27-29]. As Fig. 2 shows, the plots for zirconium, hafnium, iron, aluminum, calcium and strontium appear in the hatched band. Besides, as seen in Fig. 3, Fe-Bi-Pb-Tl and Np-In-La-lines show a straight line of slope ca. +2, showing that mutual difference of the values for these elements are larger in the HTTA system rather than in the HDEHP system. The Sc-Y-Tm-Pm-La-Ac-line of Fig. 3, however, gives a slope of +1. In all cases, it is found that these cations extractable into HTTA phase are also readily extracted into HDEHP.

Fig. 4 gives K_d values in 50% HDEHP (toluene) vs. 1, 0.1 and 0.01 N HCl systems together with K_d values in 100% TBP—1 N hydrochloric acid system. Alkali and alkaline earth metals are situated in a range of low K_d values both for the systems of HDEHP and TBP—1 N hydrochloric acid. It is very interestingthat K_d values for scandium, thorium and protactinium are very high for HDEHP, but very low for TBP. In contrast with this fact K_d values for zinc, cadmium and gold are very high for TBP, but relatively low for HDEHP. However, it is found that iron and indium have relatively high K_d values both for HDEHP and TBP.

K_d values between 50% HDEHP and 1N hydrochloric acid are plotted against the atomic number, Z, in Fig. 5. The figure shows that the K_d values vary regularly to some extent, giving two peaks in a given long period of the periodic table. A similar regularity is also found in the system of 50% HDEHP vs. 0.1 N and 0.01 N hydrochloric acid. Although an obvious exception for this regularity is the peak for iron(III), this peak may become low by adopting the K_d value for iron(II) which is more suitable for this consideration from the viewpoint of the electron configuration. Blake et al.[1] mentioned that iron(II) is less extractable. In Fig. 5, K_d values at 12 N hydrochloric acid and 100% TBP are also plotted on the same scale for comparison. It is clear and somewhat noticeable that the readily extractable ions are almost common for systems 100% TBP-12 N hydrochloric acid and 50% HDEHP-1 N hydrochloric acid. It appears as if the extraction of ions with HDEHP is not only based on chelation, but also based on partition as in the extraction with TBP. A notable exception is the case of iodine. Iodine shows remarkably high K_d values for TBP, but low for HDEHP.

As can be seen in Figs. 1 and 5, the K_d values for Ia, IIa and IIIa groups in low acidity region decrease according to the following sequence: Sc > Ca > K, Y > Sr > Rb and La > Ba > Cs. These are analogous to the sequence of relative affinity K^* for cation exchange resin Dowex 50 or Diaion SK:

$$M^{4+} > M^{3+} > M^{2+} > M^{+}$$

However, the order of the extractability with HDEHP for cations of the same valence is

* $K_{HTTA} = (MT_m)_{org} \cdot (H^+)^m_{aq} \cdot (M^{m+})^{-1}_{org} \cdot (HT)^{-m}_{org}$.

26) E. H. Huffman and L. J. Beaufait, *J. Am. Chem. Soc.*, 71, 3179 (1949).
27) R. A. Bolomy and L. Wish, ibid., 72, 4483 (1950).
28) F. Hageman, ibid., 72, 768 (1950).
29) W. W. Meinke, Progress Report 7, Univ. of Michigan, No. 1 (1958).

* $K = [MR_m]_{resin} \cdot [H^+]^m_{aq} \cdot [HR]^{-m}_{resin} \cdot [M^{m+}]^{-1}_{aq}$.

TABLE II. COMPARISON OF THE ORDER OF SELECTIVITY

Cation(III)	
HDEHQ	Sc>Tm>Y>In>Ga>Pm>Am>La>Ac, (Al)
Resin	Ac>La>·····>Dy>Y>Ho>·····>La>Sc>Al
TBP(max)	Fe, Tl>Sc>Ga>In>Yb>Tm>Er>Ho>Y>Tb>Eu,Pm,Am>Ce>La>Al
TBP	Tl>Fe>In>Ga>Al>La>Ce>Y
Cation(II)	
HDEHP	UO_2, Zn>Ga>Pb>Mn, Cu>Cd, Ni>Mg, (Ra)>Ba, Sr, Co
Resin	Ra>Ba>Pb>(Sr, Be_2O)>Ca>(Mg, Zn, Cu, Ni, Co, Mn, UO_2, Cd)>Be
TBP(max)	UO_2, Zn>Cd>Cu, Pb>Ca, Co>Mn, Mg>Ra>Ni>Ba, Sr
TBP	Zn>Cd>UO_2>Pb>Cu, Mg, Ba>Co>Mn, Ni
Cation(I)	
HDEHP	Ag>Tl>Na>K>Rb>Cs
Resin	Tl>Ag>Cs>Rb>K=NH_4>Na>H>Li
TBP(max)	Ag>Tl>Alkali metals
TBP	Ag>Tl>(K>Rb, Cs>Na)

reverse to that of the relative affinity for cation exchange resin. A similar reversal had been found in the pairs of mono(2-ethyl hexyl)-orthophosphoric acid and sulfonated cation exchange resin for selected lanthanides and actinides[29], of HDEHP and mono(heptadecyl) sulfuric acid for K, Na, and Li[30] and of phosphonic resin and sulfonic resin for K, Na and Li[31].

Table II shows the comparison of the orders of selectivity. In the table, the heading HDEHP and TBP stand for the values in the systems of 100% TBP-1 N hydrochloric acid and of 50% HDEHP-1 N hydrochloric acid, respectively. The TBP(max) for the maximum K_d values.

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30) D. F. Peppard, G. W. Mason and R. J. Sironen, *J. Inorg. Nucl. Chem.*, **10**, 117 (1959).
31) J. I. Bregman and Y. Murata, *J. Am. Chem. Soc.*, **74**, 1867 (1952).

Coloration and Decarboxylation of the Aniline Salts of 2, 4, 6-Trinitrobenzoic Acid in Ketones and Other Solvents

By Minoru HIROTA

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Molecular compounds of aromatic polynitro compounds with aromatic hydrocarbons and with aromatic amines have been reported by many authors[1] and a number of molecular compounds of 1, 3, 5-trinitrobenzene[2-4], 2, 4, 6-trinitrotoluene[5], 2, 4, 6-trinitroanisole[6], picric acid[7,8], etc., have been investigated, but little has been known of 2, 4, 6-trinitrobenzoic acid (TNBA) complexes. So the present author studied TNBA complexes and found that, while several aromatic hydrocarbons and phenols form normal molecular complexes with TNBA, aniline, as expected, forms salts when one mole of aniline is added to one mole of TNBA.

The TNBA salts of anilines decompose into the complexes of 1, 3, 5-trinitrobenzene (TNB) with anilines and carbon dioxide on heating in solution or in the crystalline state, and the decarboxylation is extremely fast in ketonic solvents even at low temperatures. Moreover, a striking dark red color is produced in ketonic solvents. From the investigation of the relation

1) Extensively reviewed by L. J. Andrews, *Chem. Revs.*, **54**, 713 (1954).
2) H. Kronberger and J. Weiss, *J. Chem. Soc.*, **1948**, 464.
3) B. R. Brown and D. L. Hammick, *J. Chem. Soc.*, **1948**, 1395.
4) H. M. Powell and G. Huse, *J. Chem. Soc.*, **1943**, 435.
5) J. Landauer and H. McConnel, *J. Am. Chem. Soc.*, **74**, 1221 (1952).
6) E. Hertel et al., *Ber.*, **61**, 1545 (1928); **63**, 2446 (1930).
7) O. L. Baril and E. S. Hauber, *J. Am. Chem. Soc.*, **53**, 1087 (1931).
8) R. Kuhn and A. Winterstein, *Helv. Chim. Acta*, **11**, 144 (1938).

between the coloration and the rates of decarboxylation in various solvents it has been found that there are two types of coloration. The color of the first type occurs immediately after the dissolution of a salt in a pure ketone, accompanying very rapid decarboxylation, its intensity decreasing rather rapidly. The color of the other type occurs some time after the dissolution of the salt in an alcohol or in a mixed solvent containing an alcohol, when the decarboxylation is completed and almost all the TNBA has decomposed, its intensity increasing gradually. The spectra of the colors of both types resemble each other in shapes but differ in the locations of the absorption maxima. The measurments of the rates of the decarboxylation of the complexes of TNBA with anilines also showed that the decarboxylation in ketones is extremely rapid.

2, 4, 6-Trinitrobenzoates of Aniline and Substituted Anilines and their Decomposition into Corresponding Trinitrobenzene Complexes on Fusion. — A colorless crystalline substance was obtained when one mole of aniline and one mole of TNBA, both in cold acetone solution, were mixed, while a red mass was obtained from one mole of TNBA and two moles of aniline. The colorless substance was proved to be a 1 : 1 compound by analysis (Found: N, 18.09%, Calcd: N, 18.30%). The infrared absorption spectrum indicated that this compound is a salt[9]; namely it showed no absorption near 1725 cm^{-1} (carbonyl stretching frequency of the carboxyl group), and 1270 cm^{-1}, but absorption bands at 1600 cm^{-1} and 1380 cm^{-1} (antisymmetric and symmetric stretching frequencies of the carboxylate ion). (See Fig. 1 for the infrared spectra of the TNBA salts of aniline and pyridine.) The molecular compounds[10] of TNBA with benzene, naphthalene and chrysene have acid type carbonyl absorptions near 1730 and 1270 cm^{-1}. The 2 : 1 compound also showed no absorption near 1730 cm^{-1} but more experiments are required for further information.

TABLE I. INFRARED SPECTRA OF TNBA AND ITS SALTS

Compound	Infrared absorption by carboxyl group, cm^{-1}		
	$\nu_{C=O}$	$\nu_{CO_2^-}$	ν_{C-O} or δ_{O-H}
TNBA	1737		1272
Sodium salt		1603	1310
Aniline salt		1603	1370
N-Methylaniline salt		1600	1348
N, *N*-Dimethylaniline salt		1600	1326
p-Toluidine salt		1597	1366
p-Anisidine salt		1605	1366
p-Bromoaniline salt		1603	1372
Pyridine salt		1602	1353

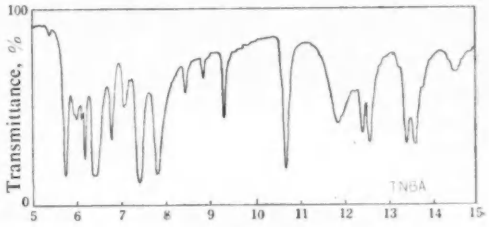


Fig. 1a.

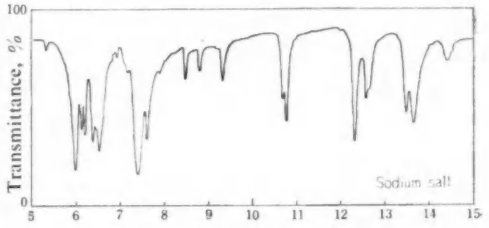


Fig. 1b.

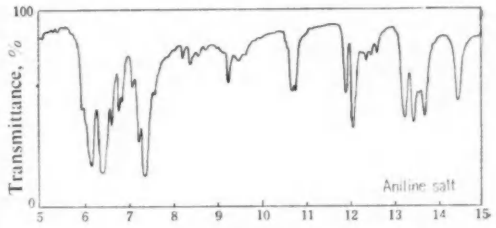


Fig. 1c.

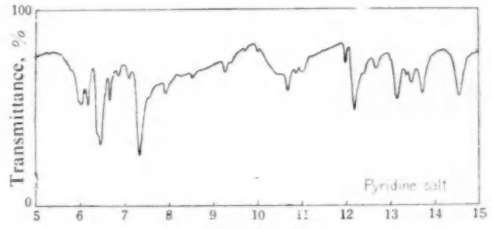


Fig. 1d.

Fig. 1. Infrared spectra of 2, 4, 6-trinitrobenzoates.

9) The salt form is proved mainly by the absence of the bands at 1730 and 1270 cm^{-1}, because the bands at 1600 and 1360 cm^{-1} overlap with the strong bands of the nitro group.

10) These molecular compounds will be described later.

2, 4, 6-Trinitrobenzoates of substituted anilines were also prepared and compared in the infrared spectra with the sodium and ammonium salts of TNBA (Table I and Fig. 1), which showed that all of these colorless 1 : 1 compounds are salts.

The 2, 4, 6-trinitrobenzoates decomposed at their melting points and changed into an orange-yellow or red liquid. The orange-yellow crystalline substance melting at 127°C, obtained from the melt of the aniline salt, was identified with the TNB-aniline complex. Other salts also gave the corresponding TNB complexes.

TABLE II. COLORATION OF ANILINE SALTS OF TNBA IN VARIOUS SOLVENTS

Solvents	2, 4, 6-Trinitrobenzoate of		
	Aniline	*N*-Monoethyl-aniline	*N*, *N*-Diethyl-aniline
Acetone	+	+	+
Methyl ethyl ketone	+	+	+
Acetophenone	+	+	+
Benzophenone	+	+	+
Cyclohexanone	+	+	+
Ethyl acetoacetate	+	+	+
Benzaldehyde	+	+	+
Acetaldehyde*	−	−	
Pinacolone	+	+	+
p-Ethylacetophenone	+	+	+
Ethanol	−	−	−
Amyl alcohol	−	−	−
Ethylene chlorohydrin		−	
Allyl alcohol	−	−	
Triethylene glycol	±	±	±
Glycerol	−	−	−
Diethylene glycol monoethyl ether	±	±	±
Ethylene bromide	−	−	−
Chloroform	−	−	−
Benzyl chloride	−	−	
Chlorobenzene	−	−	
Nitrobenzene	+	+	+
Nitromethane	+	+	+
Ether	−	−	−
Dioxane**	+	+	+
Anisole	−	−	−
Petroleum ether	−	−	−
Benzene	−	−	−
Acetic anhydride	−	−	−
Carbon disulfide	−	−	−

* 50% aqueous solution

** The color is much paler than in ketonic solvents.

The sign + is for rapid coloration, the sign ± is for slow coloration (about one hour after heating) and the sign − is for no coloration.

Coloration and Decarboxylation of the Aniline Salts of TNBA in Various Solvents. — The aniline salt of TNBA could be recrystallized from boiling benzene without coloration, but a dark red color appeared when boiling acetone was used as the solvent for recrystallization, an orange crystalline substance being obtained from the colored solution after spontaneous evaporation of acetone and was again identified with the TNB-aniline complex by the melting point and by the X-ray diffraction pattern (Table IV). On the other hand, the free TNBA could be recrystallized from boiling acetone without decomposition; and, therefore, the aniline salt form is essential for the unusual

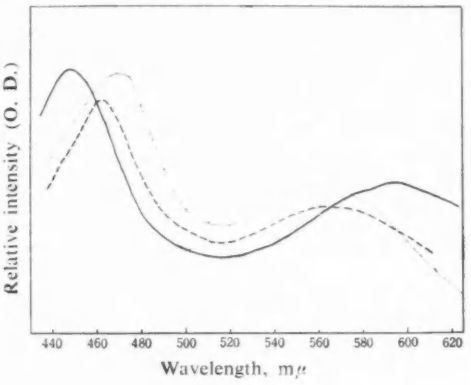


Fig. 2a.

Aniline salt of TNBA { in acetone ——; in triethylene glycol ·····; in a mixture of 60% acetone and 40% ethanol ----

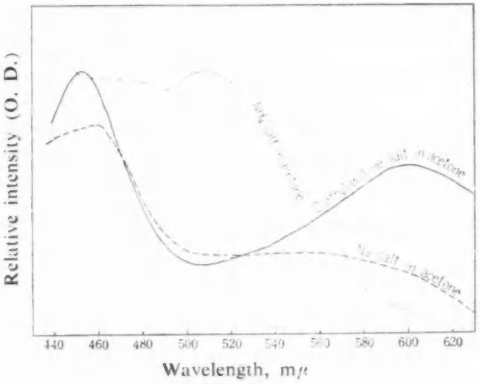


Fig. 2b.

Dimethylaniline salt ——
Ammonium salt ·····
Sodium salt ----
} in acetone.

Fig. 2. The visible spectra of TNBA salt in various solvents.

Table III. Absorption spectra of the aniline salts of TNBA

Compound	Solvent*	Absorption maxima, mμ		
TNBA-aniline	A	447.5	595	
	MEK	450	595	
	Dioxane	442.5	595	
	Triethylene glycol	470	552	
	Nitromethane	448	590	
	Ethanol	475	550(sh)	
	A90%-E10%	464	570	
	A80%-E20%	463	565	
	A40%-E60%	465	560	
TNBA-*N*-monomethylaniline	MEK	447	598	
	Ethanol	465	555(sh)	
	MEK75%-E25%	464	560	
TNBA-*N*, *N*-diethylaniline	MEK	452	605	
Na salt of TNBA	MEK	456	560(sh)	
NH_4 salt of TNBA	MEK	470	505	520(sh)
		560(sh)		

* "A" is for acetone, "MEK" for methyl ethyl ketone and "E" for ethanol.

Table IV. X-ray diffraction patterns of the decarboxylation products

Compounds	Diffraction angles, 2θ (Relative intensities)*
TNB-Aniline :	13.10(1.00), 14.26(0.22), 14.96(0.17), 18.54(0.55), 22.02(0.13), 22.75(0.11), 24.43(0.17), 25.48(0.28), 27.82(9.34), 30.55(0.15)
The decarboxylation products of TNBA salt of aniline	13.60(1.00), 14.30(0.29), 14.95(0.19), 18.60(0.82), 22.05(0.26), 22.40(0.25), 24.54(0.35), 25.52(0.50), 27.82(0.58), 30.58(0.30)

* Relative intensities to the strongest diffracted beams are in parentheses.

Table V. Results of the elementary analyses of 2, 4, 6-trinitrobenzoates

Compounds	m. p. °C	N calcd.	N found
Aniline salt	156	16.00	16.19
p-Anisidine salt	155~6	14.73	14.88
p-Bromoaniline salt	129	13.43	13.2
p-Toluidine salt	158	15.38	15.22
N-Methylaniline salt	148	15.38	15.33
N, *N*-Dimethylaniline salt	158	14.81	14.75
Pyridine salt	174	16.67	16.95

facility of decarboxylation of TNBA in ketones.

In order to investigate what kind of solvent produces the particular red color, 5 mg. of a salt was added in 2 ml. of a solvent (if insoluble, the salt was suspended in the solvent), and then the whole was heated for 5 sec. on a water bath of 60°C. If the red did not appear markedly immediately after heating, the

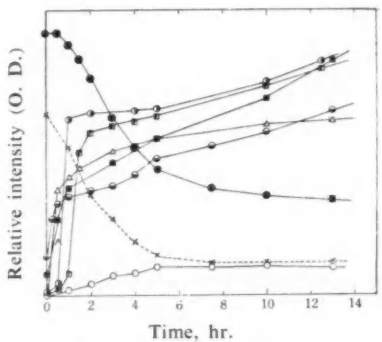
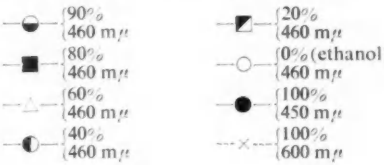


Fig. 3. Intensity change of the color produced by dissolving the aniline salt of TNBA in acetone-ethanol mixture. (at 38°C) *



* This figure shows the changes of the absorption intensities of the solutions. Time after dissolution of the salt is plotted on the horizontal axis; while the relative intensity at constant wavelength (mostly at 460 mμ) on the vertical axis. The percentages in this figure indicate volume percentages of acetone in ethanol: for example, "90%, 460 mμ" means that a mixed solvent consists of 90% of acetone and of 10% of ethanol is used for the measurement of the intensity change, and the measurement is done at 460 mμ.

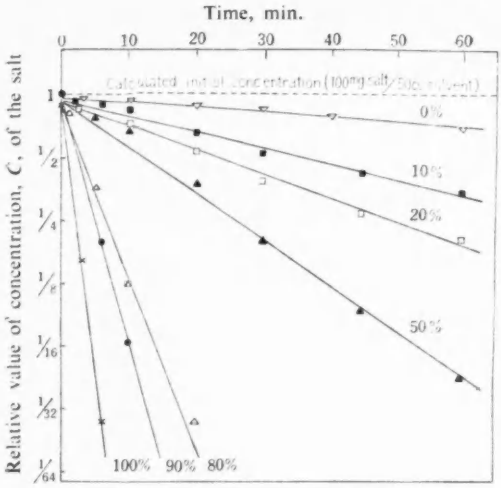


Fig. 4. Rates of decarboxylation of aniline salt of TNBA in acetone-ethanol mixed solvent.*

* The logarithmic value of relative concentration referred to the calculated initial concentration is plotted on the vertical axis. The percentages on the figure indicated acetone content in the mixture, the remainder is ethanol only.

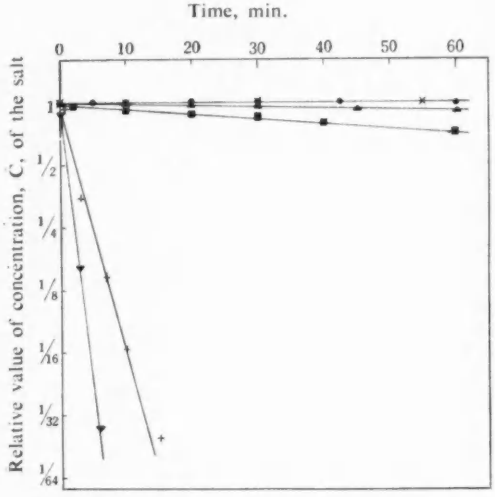


Fig. 5. Rates of decarboxylation of aniline salt of TNBA in various solvents.

—×— in water —■— in ethanol
—●— in dioxane —+— in methyl ethyl ketone
—▲— in methanol —▼— in acetone

color was observed after heating at 50°C for 3 up to 60 min.

Dark red coloration was instantly observed when a carbonyl or nitro compound was used

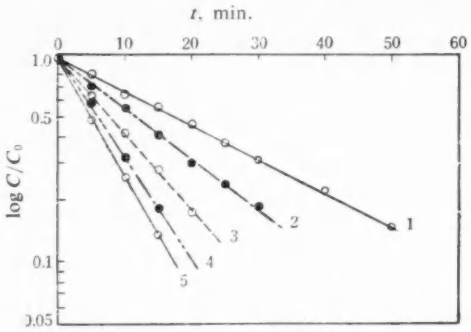


Fig. 6. The rates of decarboxylation of *p*-substituted aniline of TNBA in acetone 30°C.

C_0: intial concentration (about 0.004 mol./l.)
C: concentration at time t.
t: time after the beginning of the reaction.
1: *p*-Br, 2: *p*-NO_2, 3: *p*-Me,
4: H, 5: *p*-MeO

as the solvent. Some alcohols and ethers also produced a red color on longer heating. The color in ketones is so intense immediately after heating that very small amounts of a ketone and the aniline salts are needed for the color reaction and it gives a method for the qualitative detection of ketones. Nevertheless, this method requires ketones of high purity, so the utilization is limited. Some nitro compounds, ethers and alcohols also produced coloration, but the greenish red color in ketones and nitro compounds seemed to be different from the red color in alcohols. Results of the color reaction in various solvents are summarized in Table II.

Then, the absorption spectra of the aniline salts in various solvents were measured. Some of the spectra are illustrated in Fig. 2 and the locations of the absorption maxima are given in Table III. The spectra of the aniline salt of TNBA in a pure ketone or nitromethane, measured immediately after dissolution and warming, had absorption maxima at 447.5 and 595 mμ, and their intensities (extinction coefficients) decreased as time passed. On the other hand, the spectra of the salt in alcohols had absorption maxima at 465 and 565 mμ and their intensities gradually increased as time passed. From these experimental results it was certain that there were two types of coloration, so the time dependence of the absorption intensity was measured with the results given below.

Relation between the Rate of Decarboxylation and Coloration of the Aniline Salts of TNBA in Various Solvents.—The relation between the decarboxylation and the coloration of the TNBA salt of aniline was investigated by measuring the rate of decarboxylation and the change of

absorption intensity. The decarboxylation is extremely fast in ketones (Fig. 5). The rate of decarboxylation is in the order: acetone> methyl ethyl ketone>ethanol>methanol> dioxane. Measurements of the change of absorption intensity revealed that the intensity in pure ketones is reduced fast, while the color in the acetone-ethanol mixture, though not very intense at the beginning, becomes intense gradually. The more acetone the mixed solvent contains, the more promptly the coloration occurs, while, the more ethanol is present in the solvent, the more intense the absorption of the solution becomes. However the coloration is hardly observed in pure ethanol. On the other hand, since the decarboxylation of the aniline salt proceeds without any coloration in many other solvents at higher temperatures, the color is not essential for the decarboxylation, but the unusual facility of decarboxylation with simultaneous coloration in ketones suggests different mechanisms of the two types of decarboxylation.

The decarboxylation of the TNBA salts of substituted anilines were also examined with the results shown in Fig. 6.

To examine the nature of the intermediate compounds of the decarboxylation, the TNBA salts of some *p*-substituted anilines were prepared and the rates of decarboxylation were measured. The order of the decarboxylation rates is almost parallel to that of the coloration rates. Namely, ammonium salt $\ll$*p*-nitroaniline salt $<$*p*-bromoaniline salt $<$ aniline salt $<$*p*-anisidine salt for the coloration, and *p*-bromoaniline salt $<$*N*, *N*-dimethylaniline salt $<$*p*-nitroaniline salt $<$*N*-methylaniline salt $<$*p*-toluidine salt $<$ aniline salt $<$*p*-anisidine salt for the decarboxylation.

The order of the decarboxylation rates is not simply in the order of basicity of the anilines.

Experimental

Qualitative Tests for the Coloration. — To examine a solvent in the coloration, about 5 mg. of the aniline salt of TNBA was dissolved in 2 ml. of the solvent and the solution was heated for 30 seconds in a water bath of 60°C. If the salt was not completely dissolved, a suspension was used. All solutions in ketones produced dark red color instantly on heating. When no coloration occurred, the solution was examined after heating at 50°C for 3 minutes and 60 minutes. To test a solution in ether or other volatile solvents, the solution was heated under reflux on a water bath.

Visible Spectra of the Color. — Visible spectra were measured in the range of wavelength from 420 to 625 mμ. with a Beckman DU type quartz spectrophotometer. Determination of the band envelopes and locations of the absorption maxima were the main purpose of the spectral measurements, while the exact determination of the absolute values of intensities was less important and only relative intensities were needed for the present discussions, since the intensities of the absorption bands changed rather rapidly.

Infrared Spectra of the Salt. — The infrared spectra were determined with an Infracord infrared spectrophotometer or with a Baird Model B infrared spectrophotometer. All measurements were made in solid state; the potassium bromide pellet method was employed in most measurements, and the mull method in a few measurements. Nujol and hexachlorobutadiene were used as mulling agents, because they compensate each other, the whole wavelength region between 2.5 and 15 μ thus being covered without interference of the absorption bands of the mulling agents.

Preparation of the Materials and Determination of the Rates.—All salts were prepared by the following procedure: TNBA[12] in acetone and an equivalent amount of a base in the same solvent were mixed in an ice bath and the precipitated salt was collected by filtration as rapidly as possible, washed first with a small amount of cold acetone and then with benzene, and dried in a vacuum desiccator. The salts prepared in this way were analytically pure (Table V) and can be used in the spectral and other measurements. The rate of decarboxylation was determined by titrating the unchanged acid with a standard alkali in aqueous solution, methyl red being used as the indicator without interference by the anilines.

X-ray Diffraction Measurements.—Powder X-ray diffraction patterns were obtained with a Norelco X-ray diffractometer. Diffraction angles and relative intensities of the diffracted beams are listed in Table IV.

The author wishes to express his hearty thanks to Professor Y. Urushibara, and to Professor M. Ōki for their helpful advice and to Mr. Masuda for elementary analyses.

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11) Similar spectra are observed with TNB and 2, 4, 6-trinitroanisole in ethanol solution containing sodium ethoxide. R. Foster, *Nature*, **176**, 746 (1955); **183**, 1042 (1959).

12) 2, 4, 6-Trinitrobenzoic acid is prepared by the method described in "Organic Syntheses" [H. T. Clarke and W. W. Hartman, "Org. Syntheses", Col. Vol. I, p. 543 (1941)].

Sur la Dissolution des Minerais Sulfurés en Divers Milieux. II. Dissolution de la Pyrite et de la Chalcopyrite

Par Masami ICHIKUNI

(Reçu le 22 octobre 1959)

La décomposition ou l'altération des minerais sulfurés dépend, d'une part, de leur propre caractère, composition chimique, propriété minéralogique, structure cristalline, et d'autre part, des facteurs du milieu, température, pression, pH, potentiel d'oxydo-réduction, présence d'autres substances. Ayant exécuté des essais préliminaires, on a déjà signalé dans le rapport précédent[1] des rôles importants que jouent le pH et l'air dans la dissolution des minerais. Dans le but d'élargir et de généraliser ce résultat, on reprend l'expérience de la dissolution de la pyrite et de la chalcopyrite, classées parmi les plus importants des minéraux sulfurés primaires. L'expérience s'effectue sous les conditions oxydantes et non-oxydantes à divers pH. Les premières conditions sont caractérisées par la présence de l'air, les dernières par l'absence de l'oxygène. On met en évidence le mécanisme de la dissolution des minerais et montre sa signification géochimique. L'application du résultat du présent rapport aux phénomènes naturels sera utile pour l'éclaircissement de ces derniers.

Expérience

Généralité. — Le dispositif et les conditions de l'expérience sont les mêmes que ceux décrits dans le rapport précédent. On prend 200 ml. d'acide chlorhydrique de concentration connue ou la même quantité d'eau bidistillée dans un ballon à 300 ml., l'apporte sur un bain-marie, chauffe la liqueur à la température de 80 à 85°C, y ajoute 1 g. de minéral pulvérisé et traite pendant quatre heures, en y introduisant l'air ou l'azote avec un débit constant de 1,5 l./min. Chaque prélèvement de portion de 10 ml. doit être effectué avec l'interval d'une heure. Le dosage du fer divalent, du cuivre et du sulfate sont fait sur la liqueur filtrée.

L'interféromètre ayant indiqué 0,05% comme teneur en oxygène de l'azote, celui-ci est lavé à une solution de pyrogallol, afin d'éliminer l'oxygène.

Echantillons.—La pyrite s'est produite à la mine de Kanaborizawa, département d'Aomori, la chalcopyrite, à la mine d'Ani, department d'Akita. La dernière a été examinée par voie diffractométrique à rayons X pour qu'on vérifie qu'elle est exempte d'autres impuretés minéralogiques. Le résultat d'analyse chimique est porté sur le Tableau I. La composition chimque des échantillons se conforme approximativement à la formule chimique idéale des minéraux, FeS_2 et $CuFeS_2$. Une petite quantité d'impuretés qu'on a décelées par la spectrographie ne présentera aucun inconvénient pour l'expérience.

TABLEAU I. RÉSULTAT D'ANALYSE DES MINÉRAUX

Elément	Pyrite	Chalcopyrite
Fe	46,50%	30,40%
Cu	—	34,35
S	53,36	34,86
Total	99,86	99,61

Tout en évitant l'oxydation provoquée par la pulvérisation, on arrête cette opération lorsque toutes les poudres passent par un tamis à nombre de maille de 100.

Considérations. — (1) *Diminution du Volume de Liqueur par l'Evaporation.* — Entrainée par l'air ou l'azote introduit dans la liqueur, une portion de liqueur s'évapore. L'augmentation apparente de quantité dissoute de composants, si elle était calculée par la différence des concentrations trouvées tout en négligeant la diminution du volume, doit être supérieure à son augmentation véritable. Cela nécessite donc une correction pour la diminution du volume causée par l'évaporation. Cette correction a une importance particulière dans le cas d'un composant qui ne se dissout que très peu. Elle s'effectue par la division des concentrations trouvées par le taux de concentration, rapport du volume initial sur la somme du volume final et du volume prélevé. Toutes les concentrations trouveées ont été ainsi recalculées pour qu'on puisse éliminer l'influence de l'évaporation. Si le minéral pulvérisé contient une certaine quantité de sulfate ou d'oxyde, qui dépasse la quantité dissoute par le traitement, cela empêchera de déterminer précisément la quantité véritable de dissolution, car la correction ne se fait pas très rigoureusement. On est obligé de prendre une grande précaution pour la préparation des échantillons. On peut effectuer la correction avec une erreur inférieure à 5%.

(2) *Variation du pH.*—Lorsqu'on traite les minerais sulfurés en présence de l'oxygène, il se produit toujours une certaine quantité d'acide sulfurique et le pH de la liqueur diminue. L'effet de l'évaporation qui concentre la liqueur, par conséquent l'ion hydrogène, participe également à l'abaissement du pH. Il n'est que de 0,2, en milieu acide, avant et après le traitement, tandis que le pH descend de 6 à 3 environ par le traitement effectué avec de l'eau bidistillée. Lorsqu'on examine la relation

1) M. Ichikuni et H. Kamiya, Ce Bulletin, 32. 1368 (1959).

entre la dissolution et le pH, on prend la valeur moyenne de pH au cours du traitement, et elle est de 3,2 et de 4,2 pour le traitement effectué avec l'eau de la pyrite et de la chalcopyrite, respectivement. Pour maintenir le pH du milieu à une valeur donnée, on pourrait utiliser une solution tampon, mais son emploi offre en même temps un inconvénient, car la présence des sels étrangers exerce une influence considérable sur la dissolution des minéraux; on aura donc de la difficulté à interpréter le résultat obtenu.

(3) *Efficacité de l'Agitation.*—La réaction ayant lieu entre la phase solide et la phase liquide, l'agitation donne une influence considérable sur la vitesse de réaction. On maintient le débit du gaz à une valeur constante de 1,5 l./min., afin d'égaliser, pour toute la série d'expériences, l'efficacité de l'agitation.

(4) *Suppression du Dosage du Fer Trivalent.*—Comme la concentration de fer trivalent ne dépasse que très rarement 1% de celle de fer divalent, on a supprimé le dosage de celui-là.

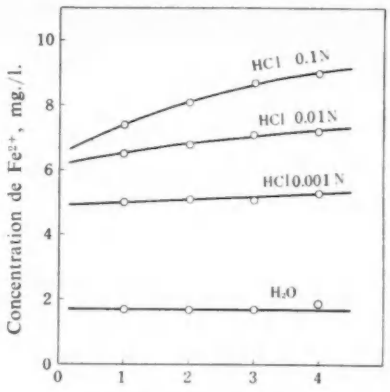

Fig. 1 Dissolution du fer à partir de la pyrite en milieu exempt d'oxygène

Résultats et Discussion

Expérience de Dissolution de la Pyrite Effectuée à l'Exclusion de l'Oxygène.—L'exclusion de l'oxygène a été réalisée par l'introduction de l'azote dans le dispositif.

Le Tableau II montre la concentration de composants qui a été correctionnée pour la diminution du volume, et qui correspond à l'heure du prélèvement et aux conditions d'expérience. L'absence de l'oxygène ne provoque presque pas la formation du sulfate, tandis que celle-ci est remarquée légèrement lors du traitement avec l'eau. Comme la pyrite est très sensible à l'oxydation en milieu à pH élevé, la formation du sulfate est attribuable à des traces d'oxygène contenu dans l'azote. Comme l'indique la Figure 1, la dissolution du fer s'accélère à mesure que le pH s'abaisse. Toutefois la courbe de concentration a une tendance à s'aplanir.

Par ces résultats, on peut exprimer la décomposition de la pyrite en milieu acide et en l'absence de l'oxygène par l'équation (1)

$$(1) \quad FeS_2 + 2H^+ \rightarrow Fe^{2+} + H_2S + S$$

L'hydrogène sulfuré étant chassé par le barbotage de l'azote, la réaction peut avancer.

TABLEAU II. VARIATION DE CONCENTRATION DE FER DIVALENT ET DE SULFATE AU COURS DE LA DISSOLUTION DE LA PYRITE

Milieu	Durée du traitement	Expérience effectuée en l'absence de l'oxygène		Expérience effectuée en présence de l'air	
	hr.	Fe^{2+} mg./l.	SO_4^{2-} mg./l.	Fe^{2+} mg./l.	SO_4^{2-} mg./l.
HCl 0,1 N	1	7,4	8	15,1	21
	2	8,1	7	21,0	26
	3	8,7	6	25,6	30
	4	9,0	6	29,6	39
HCl 0,01 N	1	6,5	6	14,4	29
	2	6,8	4	20,2	46
	3	7,1	5	25,4	60
	4	7,2	5	28,3	72
HCl 0,001 N	1	5,0	9	12,7	36
	2	5,1	10	19,6	59
	3	5,1	9	24,4	80
	4	5,3	9	28,8	102
H_2O	1	1,7	10	11,9	48
	2	1,7	13	18,2	78
	3	1,7	14	21,6	104
	4	1,9	19	24,7	129

TABLEAU III. VITESSE DE DISSOLUTION DU FER DIVALENT ET DU SULFATE À PARTIR DE 1 g. DE PYÉITE EN PRÉSENCE DE L'AIR

Milieu	Valeur moyenne de pH	Fe^{2+} m mol./hr. ($\times 10^{-2}$)	SO_4^{2-} m mol./hr. ($\times 10^{-2}$)	SO_4^{2-}/Fe^{2+}
HCl 0,1 N	1,1	1,53	1,03	0,67
HCl 0,01 N	2,0	1,78	2,80	1,57
HCl 0,001 N	2,9	1,70	4,58	2,70
H_2O	3,2	1,12	5,35	4,78

La présence de l'hydrogène sulfuré, au contraire, empêche la réaction. Pour cette raison, la pyrite reste stable en milieu acide, si le milieu est caractérisé par la présence de l'hydrogène sulfuré. Ainsi s'expliquent la stabilité et la formation de la pyrite dans la nature.

Expérience de Dissolution de la Pyrite Effectuée en Présence de l'Air.—Dans le Tableau II, on trouve que la présence de l'air favorise une dissolution considérable du fer divalent et du sulfate, et on peut constater que le potentiel d'oxydo-réduction est un facteur important pour la décomposition de la pyrite. La vitesse de dissolution du fer et du soufre dépend du pH et du potentiel d'oxydo-réduction du milieu. Il est bien connu que l'oxydation de l'hydrogène sulfuré par l'oxygène libre donne génénralement le soufre libre et non l'acide sulfurique en milieu acide[2].

En partant de l'équation (1), on a deux équations suivantes:

$$(2)\quad FeS_2 + 2H^+ + O \rightarrow Fe^{2+} + H_2O + 2S$$

où la pyrite se décompose en fer divalent et soufre libre,

$$(3)\quad FeS_2 + H_2O + 7O \rightarrow Fe^{2+} + 2H^+ + 2SO_4^{2-}$$

où tous les soufres sont oxydés en sulfate. Ces deux équations correspondent aux deux cas extrêmes de la décomposition de la pyrite, et le rapport de SO_4^{2-}/Fe peut varier de 0 à 2. Cependant au-dessus de pH 3, le fer trivalent, formé par oxydation du fer divalent, précipitant sous forme de l'hydroxyde, le rapport de SO_4^{2-}/Fe est toujours suppérieur à 2. Dans le Tableau III, on montre la vitesse de formation du fer divalent et du sulfate par la dissolution de la pyrite.

La Figure 2 montre la relation entre le pH et le rapport de SO_4^{2-}/Fe^{2+}. A un petit pH, la réaction exprimée par l'équation (2) est prédominante. Au-dessus de pH 2,5, on remarque déjà l'hydrolyse du fer trivalent, et la précipitation de l'hydroxyde devient très rapide au delà du pH 3.

Que la vitesse de formation du fer divalent et du sulfate soit variable selon le pH du milieu

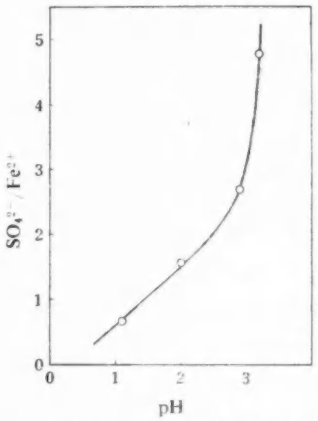

Fig. 2 Relation entre le pH et le rapport de SO_4^{2-}/Fe^{2+}, qui se trouve dans la dissolution de la pyrite.

a une signification très importante au point de vue géochimique. La variation du rapport de SO_4^{2-}/Fe en fonction du pH est influencée par les conditions d'expérience, toutefois elle garderait toujours la même tendance. Dans la nature, l'acidité forte à pH inférieur à 1 étant exceptionnelle, la désagrégation de la pyrite donne simplement l'acide sulfurique et le sulfate de fer(II). La neutralisation de la solution ainsi formée provoque la précipitation du fer, notamment l'hydroxyde de fer(III) par l'intervention de l'oxygène. L'oxydation du sulfure en sulfate se produit d'autant plus vite que le pH est plus élevé.

Expérience de Dissolution de la Chalcopyrite Effectuée à l'Exclusion de l'Oxygène.—Le Tableau IV montre le résultat de la dissolution du minéral dont l'expérience est effectuée en présence de l'azote et de l'air. Le traitement du minéral, effectué en milieu exempt d'oxygène et avec l'acide chlorhydrique, ne donne que du fer divalent et rien d'autres composants. La décomposition proposée par l'équation (4) explique bien l'indissolution du cuivre:

$$(4)\quad CuFeS_2 + 2H^+ \rightarrow CuS + Fe^{2+} + H_2S$$

On comprend que la dissolution du fer divalent est d'autant plus rapide que le pH du milieu est plus petit. D'après le Tableau

2) H. Miura, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **77**, 417 (1956).

TABLEAU IV. VARIATION DE CONCENTRATION DE FER DIVALENT, DE CUIVRE ET DE SULFATE AU COURS DE LA DISSOLUTION DE LA CHALCOPYRITE

Milieu	Durée du traitement	Expérience effectuée en l'absence de l'oxygène			Expérience effectuée en présence de l'air		
	hr.	Fe^{2+} mg./l.	Cu mg./l.	SO_4^{2-} mg./l.	Fe^{2+} mg./l.	Cu mg./l.	SO_4^{2-} mg./l.
HCl 0,1 N	1	6,8	0,36	5	47	99	9
	2	9,2	0,15	4	95	119	11
	3	10,5	0,11	4	145	136	13
	4	11,9	<0,10	4	183	150	15
HCl 0.01 N	1	6,8	<0,10	5	6,1	0,19	10
	2	9,4	<0,10	6	8,2	0,16	11
	3	10,1	<0,10	5	10,4	1,11	11
	4	10,7	<0,10	4	12,6	3,11	13
HCl 0,001 N	1	4,3	<0,10	6	5,3	<0,10	12
	2	5,3	<0,10	7	5,9	<0,10	13
	3	6,4	<0,10	7	6,9	<0,10	13
	4	7,3	<0,10	7	8,0	<0,10	15
H_2O	1	<0,5	<0,10	8	<0,5	<0,10	12
	2	<0,5	<0,10	9	0,6	<0,10	14
	3	<0,5	<0,10	9	0,9	<0,10	14
	4	<0,5	<0,10	14 ?	1,2	<0,10	14

TABLEAU V. VITESSE DE DISSOLUTION DU FER DIVALENT, DU CUIVRE ET DU SULFATE À PARTIR DE 1 g. DE CHALCOPYRITE EN PRÉSENCE DE L'AIR

Milieu	Valeur moyenne de pH	Fe^{2+} m mol./hr. ($\times 10^{-2}$)	Cu m mol./hr. ($\times 10^{-2}$)	SO_4^{2-} m mol./hr. ($\times 10^{-2}$)	Cu/Fe^{2+}
HCl 0,1 N	1,1	16,3	5,31	0,4	0,33
HCl 0,01 N	2,0	0,80	<0,63	0,2	<0,79
HCl 0,001 N	3,0	0,37	0	0,2	0
H_2O	4,2	0,11	0	0	0

IV, la vitesse de dissolution du fer est de 0,26 mg. à l'heure, dans l'acide 0,1 N, et de 0,13 mg. à l'heure, dans l'acide 0,01 N. Le fer ne se dissout aucunement dans l'eau.

Expérience de Dissolution de la Chalcopyrite Effectuée en Présence de l'Air. — Dans le Tableau IV, on voit que l'expérience effectuée en présence de l'air donne approximativement le même résultat que celle qui a été effectuée en milieu exempt d'oxygène, d'autant que le pH soit supérieur à 2. A un pH supérieur à 3, aucune dissolution du cuivre n'est remarquée, et celle du sulfate est très limitée. De ce fait on peut conclure que l'oxygène n'exerce pas une grande influence sur la dissolution de la chalcopyrite à un pH supérieur à 2. Cela se conforme au résultat du rapport précédent que la dissolution du cuivre est soumise à l'influence du pH et non du débit de l'air qu'on introduit dans la liqueur contenant du minerai pulvérisé.

Une vitesse très limitée de formation du sulfate en milieux neutre et faiblement acide attire notre attention. Pour cette raison, le traitement de la chalcopyrite avec l'eau ne diminue que modérément le pH de la liqueur. La pyrite, au contraire, diminue considérablement le pH de la liqueur, lorsqu'elle est traitée avec de l'eau, d'ailleurs chez la pyrite, la vitesse de formation du sulfate est d'autant plus grande que le pH du milieu est plus élevé. Cependant la dissolution de la chalcopyrite augmente énormément en milieu acide 0,1 N, ce qui n'est pas pareil au cas de la pyrite.

Le Tableau V montre la vitesse de formation du fer divalent, du cuivre et du sulfate par la dissolution de la chalcopyrite.

Dans le Tableau V, on trouve que la quantité dissoute de cuivre est toujours inférieure à celle de fer, quoique le rapport de Cu/Fe soit de l'unité dans le minéral. La dissolution du soufre, sous forme du sulfate, est très faible par rapport à celle du fer et du cuivre. Alors on remarque que le soufre libre se forme abondamment au cours de l'expérience effectuée en milieu acide 0,1 N. On présente donc les équations (5) et (6) qui conviendront à l'explication de ce résultat:

(5) $CuFeS_2 + 2H^+ + O \rightarrow CuS + Fe^{2+} + H_2O + S$

(6) $CuFeS_2 + 4H^+ + 2O \rightarrow$

$$Cu^{2+} + Fe^{2+} + 2H_2O + 2S$$

D'après ce résultat, on peut déduire qu'une grande dissolution du cuivre à partir de la chalcopyrite est peu possible, d'autant que le minéral se trouve indépendamment des autres minéraux, et que le milieu en question ne soit pas très acide et oxydant. Cependant on trouve souvent une dissolution rapide du cuivre à partir du gisement des minerais sulfurés. On ne pourra pas éclaircir ce phénomène sans avoir recours aux effets de la co-présence d'autres minéraux, notamment de la pyrite, et de l'action de l'acide sulfurique ou du fer, qui sont produits par la désagrégation des minerais sulfurés. D'après Ohashi[3], la présence de la pyrite ne favorise pas particulièrement la dissolution du cuivre à partir de la chalcopyrite, toutefois le fer trivalent contribue à sa dissolution, en réagissant sur le minéral.

Les effets de la co-présence d'autres minéraux sur la dissolution de la chalcopyrite présentent un problème intéressant, car on a déjà désigné la présence d'autres substances comme un des facteurs importants déterminant le milieu géochimique.

Désagrégation de la Pyrite dans la Nature

L'acide sulfurique et le sulfate de fer se forment en grande quantité par la désagrégation des minerais sulfurés. C'est ainsi que les eaux d'une forte acidité, souvent de pH inférieur à 3, jaillissent au fond de mine. Ces eaux se jettent dans une rivière, et abaissent dans une grande mesure le pH des eaux de rivière. Il est d'un intérêt particulier de comparer le résultat de ces expériences avec celui d'analyse des eaux de mine.

On a choisi donc à partir des résultats d'analyses des eaux de mine de Kamikita, département d'Aomori,[4] les eaux contenant simplement de l'acide sulfurique et du sulfate de fer. Le résultat d'analyse des dernières est indiqué par le Tableau VI.

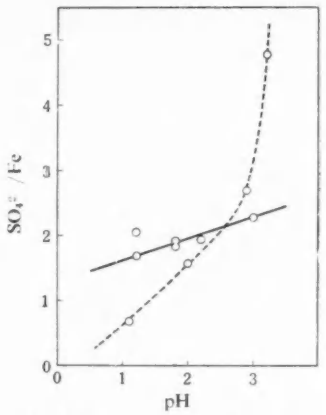

Fig. 3 Relation entre le pH et le rapport de SO_4^{2-}/Fe, qui se trouve dans les eaux de mine de Kamikita (courbe discontinue correspondant à celle de la Fig. 2).

Avec les chiffres du Tableau VI, on examine la relation entre le pH et le rapport de SO_4^{2-}/Fe, et la compare avec celle obtenue par les expériences décrites ci-dessus. La Figure 3 montre cette comparaison. On en a constaté que :

1. A mesure que le pH s'abaisse, le rapport de SO_4^{2-}/Fe a une tendance à diminuer, mais il n'est pas très inférieur à 2, même à pH 1.

2. Cela souligne que la réaction exprimée par l'équation (3) est toujours prédominante dans la nature, même à un petit pH, par conséquent la formation abondante du soufre libre par la désagrégation de la pyrite serait peu possible.

La relation entre le pH et le rapport de SO_4^{2-}/Fe, qui se trouve dans les données du Tableau VI, ne se conforme pas à celle obtenue par les expériences. Cette discordance peut s'expliquer par le fait que dans la nature, la manière de contact des minerais avec l'air est entièrement différente de celle effectuée au laboratoire, et que la dissolution des minerais est soumise à l'influence des substances

TABLEAU VI. QUELQUES RELEVÉS DES DONNÉES D'ANALYSE DES EAUX DE MINE DE KAMIKITA, DÉPARTEMENT D'AOMORI (D'APRÈS T. HAMACHI ET H. GOTO)

pH	Fe^{2+} m mol./l.	Fe^{3+} m mol./l.	SO_4^{2-} m mol./l.	SO_4^{2-}/Fe total
1,2	107	95,8	340	1,68
1,2	182	80	535	2,04
1,8	15,0	9,5	46,4	1,89
1,8	22,7	0	42,2	1,86
2,2	9,3	0,7	19,4	1,94
3,0	5,0	3,8	20,1	2,28

3) S. Ohashi, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **74**, 845 (1953).

4) T. Hamachi et H. Goto, *Bull. Geol. Survey Japan*, **6**, 265 (1955).

co-existantes. Au laboratoire on effectue le barbotage de l'air, mais une agitation violente de solution est plutôt rare dans la nature, par conséquent l'hydrogène sulfuré ne sera pas chassé hors de solution, même s'il s'est formé. D'ailleurs la relation entre le pH et le rapport de SO_4^{2-}/Fe peut varier selon la manière d'introduction de l'air.

Dans le Tableau VI, on trouve qu'il y a une quantité considérable de fer trivalent dans les eaux, et que l'acidité des eaux consiste en acide sulfurique, ce qui n'est pas pareil aux conditions d'expérience où l'acidité consiste en acide chlorhydrique. Il faut qu'on tienne compte de la présence du fer trivalent et de l'acide sulfurique pour l'explication complète du phénomène de désagrégation des minerais sulfurés. Toutefois il est d'une signification particulière qu'on a pu ici reproduire d'une façon réduite le phénomène de désagrégation.

L'auteur exprime ses remerciements sincères à Monsieur le professeur K. Noguchi qui a bien voulu lire cet essai et lui donner des conseils utiles, et particulièrement à Monsieur H. Kamiya dont le concours aimable et l'encouragement étaient indispensables pour la réalisation de ce travail. Il remercie également Monsieur le professeur T. Watanabe et Monsieur le docteur A. Kato, à l'Université de Tokyo, pour l'examen diffractométrique à rayons X de la chalcopyrite.

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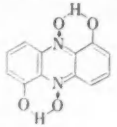
The Constitution of the Pigments of Brevibacterium Crystalloiodinum, Sasaki, Yoshida et Sasaki

By Tosi Irie, Etsuro Kurosawa and Iwao Nagaoka

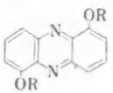
(Received January 14, 1960)

Sasaki, Yoshida and Sasaki[1] isolated a deep purple, antibiotic pigment and a yellow pigment from the culture medium of *Brevibacterium crystalloiodinum*, Sasaki, Yoshida et Sasaki*, and named them crystalloiodinine A and B, respectively. The name of crystalloiodinine was proposed on account of the purple pigment resembling to iodinine[2].

The present paper is concerned with the study on the structure of these pigments, which were sent by Professor Yuji Sasaki, to whom the authors' thanks are due. It has been established that crystalloiodinine A is identical with iodinine, *i.e.*, 1,6-dihydroxyphenazine di-*N*-oxide (I), and crystalloiodinine B is 1,6-dihydroxyphenazine (II: R=H).



(I)



(II)

The purple pigment, isolated from the culture medium, was purified by repeated recrystallizations from chloroform or dioxane; its homogeneity was indicated by the fact, that it gives a single blue band on alumina chromatogram. Crystalloiodinine A, $C_{12}H_8O_4N_2$, was thus obtained in deep purple prisms with coppery lustre, m.p. 230°C (decomp.). It dissolves in aqueous sodium hydroxide to a blue solution, and separates in purple crystals when the alkaline solution is acidified. It shows greenish coloration in ethanol with ferric chloride. The ultraviolet spectrum in chloroform shows maxima at 291 mμ ($\log \varepsilon = 5.1$) and 355 mμ ($\log \varepsilon = 3.9$) (Fig. 1); and the infrared spectrum exhibits absorptions due to a bonded hydroxyl group at 3400 cm^{-1} and that of *N*-oxide group at 1285, 1160 and 1025 cm^{-1} (Fig. 2). The infrared spectrum and certain chemical properties[1] indicated, that the pigment closely resembles iodinine[2-6]. Accordingly, crystalloiodinine A

1) Y. Sasaki, T. Yoshida and H. Sasaki, presented at the Meetings of the Society of Agricultural Chemistry of Japan, Sapporo, Nov. 21, 1957 and Tokyo, April 4, 1959.
2) G. R. Clemo and H. McIlwain, *J. Chem. Soc.*, **1938**, 479.
* This new species of *Brevibacterium* was isolated at the Faculty of Agritculture of Hokkaido University by Prof. Y. Sasaki and his collaborators[1].
3) G. R. Clemo and A. F. Daglish, *J. Chem. Soc.*, **1950**, 1481.
4) A. I. Kiprianov, S. B. Serebryanyi and V. P. Chernernetskii, *Doklady Akad. Nauk. S. S. S. R.*, **69**, 651 (1949); *Chem. Abstr.*, **46**, 4010 (1952).
5) S. B. Serebryanyi, V. P. Chernetskii and A. I. Kiprianov, ibid., **70**, 645 (1950); *Chem. Abstr.*, **45**, 4249 (1951).
6) I. Yoshioka and Y. Kidani, *J. Pharm. Soc. Japan*, **72**, 1301 (1952).

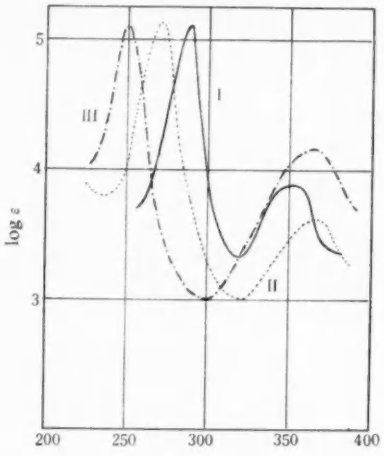


Fig. 1. Absorption spectra of:
I. crystalloiodinine A and 1, 6-dihydroxyphenazine di-*N*-oxide (in chloroform),
II. crystalloiodinine B (in ethanol),
III. acetate of crystalloiodinine B (in ethanol).

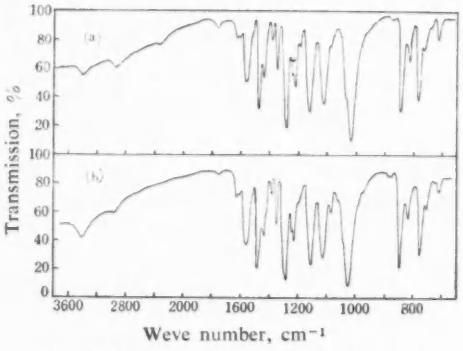


Fig. 2. IR spectra in KBr of (a) crystalloiodinine A and (b) 1, 6-dihydroxyphenazine di-*N*-oxide.

has been found to be identical with 1, 6-dihydroxyphenazine di-*N*-oxide, which was synthesized after Yoshioka and Kidani[6], by the mixed melting point method and by comparison of ultraviolet** and infrared spectra (Figs. 1 and 2).

On hydrogenating the pigment over Adams platinum catalyst, golden yellow plates, $C_{12}H_8O_2N_2$, m. p. 273~4°C (diacetate: pale yellow needles, m. p. 234°C) were yielded. This

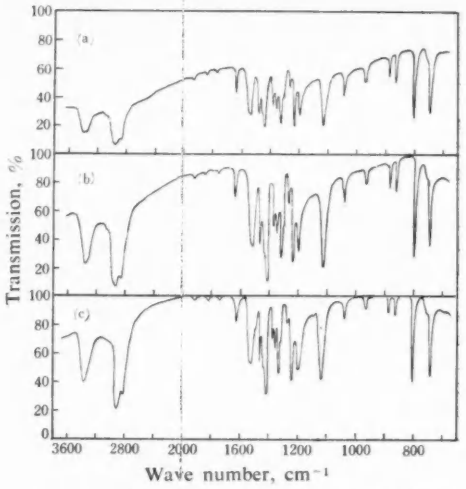


Fig. 3. IR spectra in nujol of (a) reduction product of crystalloiodinine A, (b) crystalloiodinine B, and (c) 1, 6-dihydroxyphenazine.

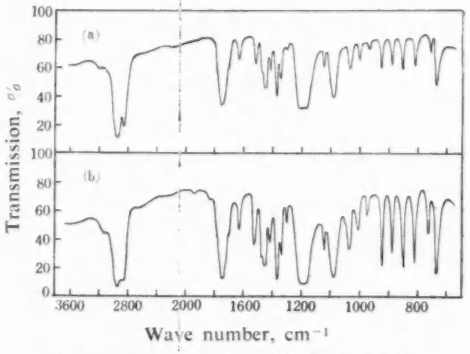


Fig. 4. IR spectra in nujol of (a) diacetate of crystalloiodinine B and (b) 1, 6-diacetoxyphenazine.

material has been identified as 1, 6-dihydroxyphenazine[7] as described below.

The yellow pigment, isolated from the culture medium, was also purified by the chromatographical method and recrystallization from benzene or sublimation under reduced pressure. Crystalloiodinine B, $C_{12}H_8O_2N_2$, was obtained in golden yellow plates, m. p. 273~4°C. It dissolves in aqueous sodium hydroxide to a purplish-red solution and separates in yellow crystals on acidification of the alkaline solution. It shows greenish coloration in ethanol with ferric chloride. The ultraviolet spectrum in ethanol shows maxima at 274 mμ ($\log \varepsilon = 5.1$) and 370 mμ ($\log \varepsilon = 3.6$) (Fig. 1); and the infrared spectrum exhibits absorption due to a

** The ultraviolet spectrum does not agree with that shown in the literature.[2]

7) I. Yoshioka and Y. Kidani, ibid., **72**, 847 (1952).

hydroxyl group at 3390 cm^{-1}, but does not exhibit an *N*-oxide band (Fig. 3). Diacetate of this pigment, $C_{16}H_{12}O_4N_2$, was obtained in pale yellow needles, m. p. 234°C (the ultraviolet and infrared spectra are shown in Figs. 1 and 4, respectively). Thus, by the mixed melting point method and by comparison of the absorption spectra of the pigments and of their diacetates, it has been established that crystalloiodinine B is identical with the above reduction product of crystalloiodinine A and with 1,6-dihydroxyphenazine.

It is possible to assume that 1,6-dihydroxyphenazine, which has not hitherto been isolated from any natural source, plays the role of a precursor of iodinine[1].

Experimental

Isolation of the Pigments. (1) Purple Pigment, Crystalloiodinine A.—The bacteria were incubated in the broth containing 1% glycerine. The cultures were shaken at 30°C for 5 days, during which deep purple crystals developed. Water was added to the cultures and shaken, and the washings were allowed to stand. After 24 hr. the suspension of bacteria was decanted from precipitated pigment. Several treatments were sufficient to remove the pigment. The crude pigments were filtered and extracted in a Soxhlet apparatus with chloroform. On concentration, the pigment separated as purple prisms with coppery lustre; it was recrystallized from chloroform or dioxane, m. p. 230°C (decomp.). Qualitative tests showed the pigment to contain nitrogen; sulfur and metals were absent.

Found: C, 58.61; H, 3.43; N, 11.42. Calcd. for $C_{12}H_8O_4N_2$: C, 59.02; H, 3.30; N, 11.48%.

It was slightly soluble in chloroform, carbon disulfide, petroleum ether, glacial acetic acid, acetone, dioxane and benzene, but not soluble in water, ethenol, nor ether. It was soluble in concentrated sulfuric acid with blue-greenish coloration, and also in aqueous sodium hydroxide with blue coloration. It showed greenish coloration in ethanol with ferric chloride. It dissolved in glacial acetic acid to give a red solution, which on warming with the addition of 10% potassium iodide liberated iodine.

This compound was found to be identical with 1,6-dihydroxyphenazine di-*N*-oxide, which was synthesized after Yoshioka and Kidani[6], by the mixed melting point method and by comparison of their absorption spectra.

(2) Yellow Pigment, Crystalloiodinine B.—The water layer obtained by decantation to remove crystalloiodinine A, was acidified by hydrochloric acid and extracted with ether. After evaporation of the ether, black gruel was obtained. This was treated with a small amount of chloroform and filtered. Dark brown crystals were boiled with benzene and filtered. Evaporation of the solvent afforded yellow crystals, which were recrystallized from benzene or sublimated under reduced pressure. Golden yellow plates were obtained, m. p. 273~4°C.

Found: C, 67.98; H, 3.53; N, 13.12. Calcd. for $C_{12}H_8O_2N_2$: C, 67.97; H, 3.80; N, 13.28%.

This material was soluble in benzene, alcohol, and ether. It was soluble in concentrated sulfuric acid with greenish coloration and also in aqueous sodium hydroxide with purplish-red coloration. It showed greenish coloration in ethanol with ferric chloride.

This compound was identified as 1,6-dihydroxyphenazine[7] by the mixed melting point method and by comparison of absorption spectra with an authentic specimen.

Reduction of Crystalloiodinine A.—The pigment (0.6 g.), platinum oxide (0.6 g.) and absolute ethanol (50 cc.) were shaken in hydrogen (1 atm.) for 24 hr., during which the pigment completely dissolved. Catalysts were then filtered off. On being exposed to air, the color of the filtrate changed soon from pale orange to yellow. This meant, that the hydrogenation yielded the dihydrophenazine compound and it was oxidized by air to the corresponding phenazine derivative. After evaporation of the solvent under reduced pressure, dark brown crystals were obtained. On purification by recrystallization from benzene or sublimation under reduced pressure, golden yellow plates were yielded, m. p. 273~4°C. This material was found to be identical with 1,6-dihydroxyphenazine and crystalloiodinine B, by the mixed melting point method and by comparison of the absorption spectra.

Found: C, 67.48; H, 3.45; N, 13.08. Calcd. for $C_{12}H_8O_2N_2$: C, 67.97; H, 3.80; N, 13.28%.

Acetylations of the Reduction Product and Crystalloiodinine B.—The compound (50 mg.), pyridine (5 cc.), and acetic anhydride (1 cc.) were refluxed for 2 hr. The solvent was removed under reduced pressure and the residue was recrystallized from ethanol. Pale yellow needles were obtained, m. p. 234°C. This compound was found to be identical with an authentic specimen of 1,6-diacetoxyphenazine (II: R=$COCH_3$) by the mixed melting point method and by comparison of the absorption spectra.

Found: C, 64.58; H, 3.86; N, 9.50. Calcd. for $C_{16}H_{12}O_4N_2$: C, 64.86; H, 4.06; N, 9.46%.

The authors are indebted to Mr. Y. Ichinoe for measurements of absorption spectra and to Mr. H. Homma of the Institute of Physical and Chemical Research, Tokyo, for microanalyses.

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Dilatometric Study on Transition Phenomena of Various Polyethylenes with Different Degree of Chain Branching

By Kōji TANAKA

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Much interesting work has been done about the effect of chain branching of polyethylene on its physical and chemical properties. It is well known that branches in ordinary high-pressure polyethylene are of two types, short chain and long chain branchings. According to Roedel[1] short chain branching has the most marked effect on such properties as melting point, yield point, bending modulus, hardness, and vapour permeability, while long chain branching has a marked effect on melt flow and viscoelastic properties. Richards[2] presented data on the relation between the degree of crystallinity and the degree of short chain branching in a series of polyethylenes, and Sperati et al.[3] gave quantitative relations between density, degree of chain branching, and degree of crystallinity, and also between density and many other physical properties.

An early study of polyethylene by volume dilatometry was carried out by Boyer and Spencer[4]. They found melting points at 103°C and in the neighborhood of 115°C for different polyethylenes. Hunter and Oakes[5] reported from the volume measurement of a number of polyethylenes in the range from 0° to 170°C that the percentage of crystalline part did not change up to about 70°C, but thereafter fell more and more rapidly until the substances became wholly amorphous at a temperature depending on the nature of the specimen and that density of molten polyethylene showed little dependence on average molecular weight, but the temperature at which crystalline material first appeared on cooling was raised by increase in molecular weight. Mandelkern and his coworkers[6] presented the results of a study of volume-temperature behavior and melting temperatures of linear polymethylene and highly branched polyethylene. For polymethylene a well defined first order transition or melting temperature was found at 136.5±0.5°C and 70% of melting occurred in only a three to four degree interval, while for branched polyethylene the melting temperature was 115°C and the melting range considerably extended in comparison with the linear polymethylene. Similar results were reported by Nielsen[7] and recently by Marker[8] as for the melting of polyethylene. Grams and Gaube[9] showed that melting temperature existed between 124° and 133°C for low-pressure polyethylene and between 104° and 111°C for high-pressure polyethylene. According to the results by Hunter and Oakes, and by Nielsen, specific volumes above melting point were equal for various polyethylenes at the same temperature, but according to Grams and Gaube high-pressure polyethylene had higher specific volume than low-pressure polyethylene. Gubler and Kovacs[10] determined the specific volume of three samples (high-pressure, Ziegler and Marlex) dilatometrically between −38.8° and 170°C after various heat treatments, and showed the variation of the degree of crystallinity with temperature, the size of the polyethylene crystal and the state of the distribution of the crystal. About the specific volume above melting point they also showed that all the polyethylenes had the equal specific volumes at the same temperature regardless of the properties of polyethylenes. Moreover they showed that the cubic expansion coefficient changed at the temperature between −20° and −25°C for high-pressure polyethylene and Ziegler polyethylene, which was well consistent with the result presented by Danusso et al.[11]

Now, according to Hunter and Oakes as is mentioned already, molecular weight is given as a factor affecting the properties such as melting point, crystallizing temperature, that is, the temperature at which crystalline material first appears on cooling, and premelting phenomenon. However, by the appearance of polyethylene made by the low-pressure process and from the

1) M. J. Roedel, *J. Am. Chem. Soc.*, **75**, 6110 (1953).
2) R. B. Richards, *J. Appl. Chem.*, **1**, 370 (1951).
3) C. A. Sperati, W. A. Franta and H. W. Starkweather, Jr., *J. Am. Chem. Soc.*, **75**, 6127 (1953).
4) R. F. Boyer and R. S. Spencer, *J. Appl. Phys.*, **15**, 398 (1944).
5) E. Hunter and W. G. Oakes, *Trans. Faraday Soc.*, **41**, 49 (1945).
6) L. Mandelkern et al., *J. Am. Chem. Soc.*, **75**, 4093 (1953).
7) L. E. Nielsen, *J. Appl. Phys.*, **25**, 1209 (1954).
8) L. Marker, R. Early and S. L. Aggarwal, *J. Polymer Sci.*, **38**, 369 (1959).
9) E. Grams and E. Gaube, *Angew. Chem.*, **67**, 548 (1955).
10) M. G. Gubler and A. J. Kovacs, *J. Polymer Sci.*, **34**, 551 (1959).
11) F. Danusso, G. Moraglio and G. Talamini, ibid., **21**, 139 (1956).

several reports above quoted, it seems that chain branching must be regarded as a more significant factor affecting those properties. But at present detailed data about this point are not yet available.

Therefore a series of measurements were performed in the present paper about melting point, crystallizing temperature, premelting phenomenon, glass transition temperature, and degree of crystallinity at 25°C for various polyethylenes with different degrees of short chain and of long chain branchings. The results obtained showed that the temperature and degree crystallinity were raised with the increase of short chain branching. About the effect of long chain branching, no remarkable result could be found, since the amount of long chain branching contained in the sample used was very small.

Sample.—Samples used in this investigation were Marlex 50-9, Ziegler polyethylenes, and eight kinds of high-pressure polyethylenes. These high-pressure samples were provided by the courtesy of Dr. Hammer of E. I. du Pont de Nemours and Company. These samples, the molecular parameters of which are listed in Table I, were different in molecular weight, melt index, degree of short chain branching and that of long chain branching. Marlex 50-9 and Ziegler polyethylene were commercially available polymers made by Phillips Petroleum Company and The Dow Chemical Company, respectively. As the molecular parameters for these samples were not available, the degree of short chain branching was determined by the infrared method by using the 1370 and 1378 cm^{-1} bands according to Slowinski[12]. It was found to be 0.25 for Marlex 50-9 and 0.4 for Ziegler polyethylene.

TABLE I. THE MOLECULAR PARAMETERS[a] FOR POLYETHYLENE SAMPLES

Sample	Melt index	$M_n \times 10^{-3}$	N_c[b]	N_w[c]
A[d]	0.2	34	1.6	20
B	2.1	32	1.6	18
C	2.1	21	2.2	27
D	2.1	18	3.0	34
E	3.8	20	1.6	13
F	2.0	50	2.0	18
G	1.8	27	0.6	10
H	16.0	12	3.2	29
Marlex 50-9			0.25[e]	
Ziegler			0.4[e]	

a) These were determined in E. I. du Pont de Nemours and Company by the methods described in J. Am. Chem. Soc., **75**, 6110 (1953).
b) Short chain branching index in CH_3 groups per 100 CH_2 groups.
c) Long chain weight average number of branch points per molecule. According to Bunn*, polyethylene has generally a relatively small number of long chain branches, 8-10 per molecule on a weight average basis and this is equivalent to less than one per molecule on a number average basis.
* C. W. Bunn, Polythene, A. Renfrew and P. Morgan, eds., Iliffe, London, Interscience, New York, 1957, Ch. 7.
d) These (A to H) are high-pressure polyethylenes.
e) This was determined here by the infrared method.

Experimental

An experiment was carried out by volume dilatometry on which there was detailed description by Bekkedahl[13].

The dilatometer used in this experiment was made of Pyrex glass (as the volume expansion coefficient 0.00001/deg. was used) and consisted of three parts (Fig. 1, a). They were connected together tightly

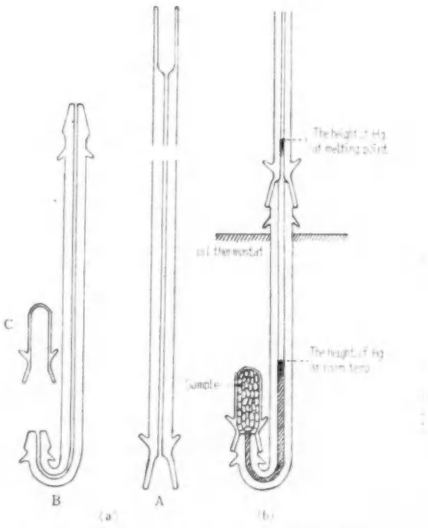

Fig. 1. Dilatometers: (a) for the measurements from about −40° to 150°C. (b) for the measurements above melting point.

with springs and in the case of measurement the dilatometer was immersed into the bath up to the height a little below the ground joint connecting the parts A and B. Prior to the experiment the capillary of part A was calibrated. After the dried and weighed sample was put in part C and this part was combined with part B, they were weighed, and then they were connected to the apparatus shown in

12) E. J. Slowinski, Jr., H. Walter and R. L. Miller, ibid., **19**, 353 (1956).
13) N. Bekkedahl, *J. Research Natl. Bur. Standards*, **42**, 145 (1949).

Fig. 2 and all the ground parts greased with silicone grease. Mercury as the confining liquid was inserted by distillation under vacuum of 10^{-3} mmHg and finally the total weight was weighed again in order to known the amount of mercury. As this amount of mercury was insufficient for the measurement, the adequate amount of mercury was weighed and added after parts A and B were combined together. The specific volume of the sample at the fixed temperature was calculated from the weights of the sample and of mercury and the total volume of parts B and C of the dilatometer which had been determined by using mercury in advance. In the case of calculation, corrections for the emergent stem and the expansion or contraction of the glass of the dilatometer were made according to Bekkedahl.

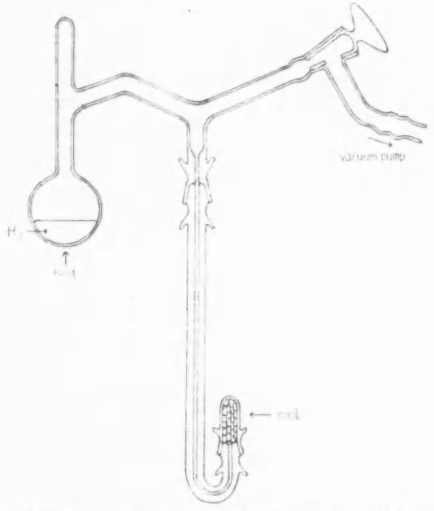

Fig. 2. The apparatus for insertion of Hg by vacuum distillation.

As is well known, the specific volume of polyethylene is dependent on temperature, as well as on its crystallinity and the amorphous region may have the possibility of further crystallization at temperature above its glass transition temperature, if the sample is not sufficiently crystallized. Therefore it is naturally expected that the volume-temperature curve above the glass transition temperature obtained by heating such a specimen contains both effects of the increase of volume by thermal expansion and the decrease of volume by further crystallization, which will obstruct the reproducibility of the curve and complicate the analysis of it. In order to eliminate such disadvantages, volume-temperature curves were taken for sufficiently crystallized samples. Sufficient crystallization of samples was carried out as follows. (1) The height of mercury in the capillary of the dilatometer containing the untreated polyethylene and mercury was recorded at 25°C exactly to 0.001 cm. (2) The dilatometer was gradually heated in the oil thermostat up to 150°C and kept at that temperature for about three hours to melt the sample in the dilatometer. (3) It was then cooled down slowly at the rate of 1/5°C per min. to 25°C. (4) The height of the mercury column was again recorded at 25°C. In this case the height was lower than that in the former case, which showed that the volume of the sample decreased by further crystallization by this treatment. Similar operations were performed, the time of melting being lengthened or shortened and the cooling rate being slower or faster, and also the dilatometer being kept for several hours at the temperature where crystallization occurred, on the way back to 25°C from 150°C at the rate of 1/5°C per min. The height of the mercury column thus obtained at 25° was equal to or higher than that obtained by the already mentioned way. As the result it is considered that the polyethylene sample can be crystallized to the highest degree by this procedure, and all the most highly crystallized specimens of polyethylene used for this investigation were obtained in this way. Volume temperature measurements were repeatedly performed in two temperature ranges, from 40°C to around freezing point of mercury and from 20° to 150°C. For measurements below 40°C a Dewar vessel containing toluene was used as a bath. The bath temperature was lowered about 5°C at a time by throwing pieces of dry-ice into the bath and it was kept at constant temperature for 15 min. by controlling the fluctuation of temperature ± 0.05°C. After that the bath temperature and the height of mercury column which corresponded to the volume change by cooling of the dilatometer contents, polyethylene and mercury, were recorded. It was confirmed that 15 min. was sufficient for polyethylene to attain the equilibrium temperature within the experimental error. Similar operations were taken down to the melting point of mercury. After the measurement at the lowest temperature was finished, the bath temperature was raised by inserting nichrom wire into the bath and measurements were performed in quite the same way up to 40°C. The temperature control of the bath was carried out by letting toluene chilled below the bath temperature run through the cooling pipe immersed in the bath. The current of chilled toluene was regulated so that it might be turned off or on automatically according to the change of the bath temperature.

The measurements from 20° to 150°C were performed in the oil thermostat which was used for thermal treatment of the sample and carried out in the same way as the measurements below 40°C except in the case of the temperature range around melting point of polyethylene. In the vicinity of the melting point of the specimen the height of mercury column abruptly increased owing to the expansion of the sample by premelting or melting, so the bath temperature was raised 1°C at a time and a sufficiently long time was taken until the sample ceased to expand. When the measurement was finished at 150°C, the dilatometer was kept at the temperature for three hours, and then cooled slowly down to 25°C at the rate of 1/5°C per min. to crystallize sufficiently the sample again, and the experiment was repeated. In this case the measurements were carried out around the melting point of the sample at a one degree intervals, in order to

know exactly the crystallizing temperature. Experiments of these kinds were repeated two or three times for each sample.

Result and Discussion

The specific volume-temperature curves from around −40° to 150°C for the most highly crystallized polyethylenes are shown in Fig. 3.

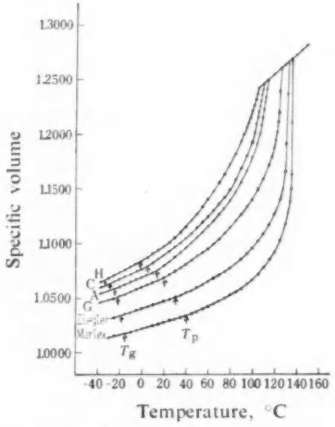

Fig. 3. Specific volume-temperature curves of the most highly crystallized polyethylenes from about −40° to 150°C. Those of samples B, D, E and F are omitted to avoid confusion.

As was mentioned already, the volume-temperature measurements were performed separately, covering two temperature ranges, below 40°C and above 20°C. The two curves obtained in these temperature ranges coincided perfectly between 20° and 40°C.

As is shown in the figure, the sample having the higher degree of short chain branching has the higher specific volume in the temperature range below melting point. Samples A, B and E which are equal in degree of short chain branching have almost equal values of specific volume at each measured temperature. This results shows that the highest degree of crystallinity of polyethylene is dependent upon the degree of short chain branching as was reported already by Richards. By inferring from the fact that when they are annealed, the unbranched linear polymethylene gets a considerably high degree of crystallinity and the more or less branched polyethylene has a lower one, it is considered that most of the amorphous regions of the most highly crytsallized polyethylene arises from the existence of short chain branching and branch point of long chain branching which disturb the regularity of molecules and keep the molecules from being

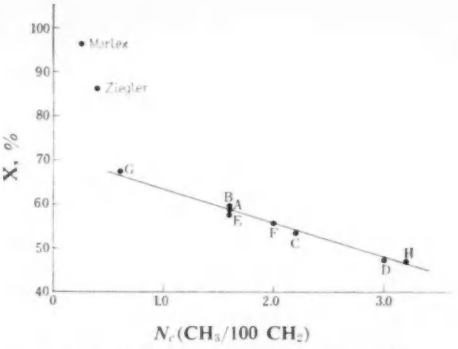

Fig. 4. The relation between degree of short chain branching and degree of crystallinity.

arranged in good order in proportion to their number. Therefore polyethylene containing the larger amount of chain branching is considered to have the poorer degree of crystallinity, even if it has the highest degree of crytallinity.

The highest degree of crystallinity of polyethylene samples at 25°C are illustrated in Fig. 4 as a function of short chain branching. They were obtained transforming the following equation, as was done by Kuroda et al.[14],

$$X=\frac{V-V_l}{V_c-V_l} \tag{1}$$

where V was the specific volume of the sample directly obtained from the volume-temperature measurement, V_l the specific volume of purely amorphous region, and V_c that of the entirely crystalline region. According to Gubler and Kovacs, V_l and V_c are expressed as follows;

$$V_l=1.170+9\times10^{-4}(T-25) \tag{2}$$

and

$$V_c=1.0255+3\times10^{-4}(T-25) \tag{3},$$

where T shows temperature in °C. The relation between V and T at any degree of crystallinity is shown by a straight line by putting V_l, V_c above presented and optional value for X into the equation (1). For the values 0.0, 0.1, 0.2, ... 0.9 and 1.0 of X, a series of $V-T$ line was obtained (Fig. 5) and from these straight lines and specific volume-temperature curve of polyethylene the degree of crystallinity was estimated.

A curve similar to that shown by Richards was obtained as a whole between the degree of crystallinity and the degree of short chain branching. According to the equations presented by Sperati et al. which showed the relation

14) T. Kuroda et al., given out in the symposium on polyethylene in Tokyo, November 1959.

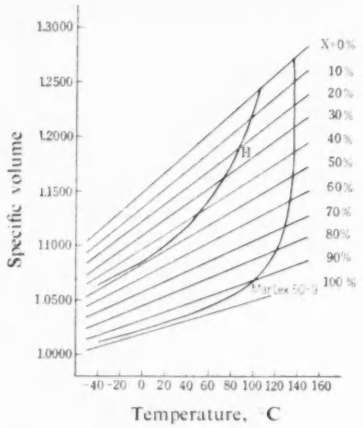

Fig. 5. The relationship between specific volume and temperature in various degree of crystallinity from which the degree of crystallinity of polyethylene was estimated.

between the density and the degree of crystallinity and that between the density and short chain branching, the linear relation is formed between the degree of crystallinity and the degree of short chain branching in the range of CH_3/100C from 0.4 to 5.0 and within the accuracy of $\pm 1.0\%$. In this experiment the linear relation was also obtained in the range of degree of short chain branching within the same accuracy shown by Sperati et al., though the slope of the straight line differed from that obtained by them. Marlex and Ziegler polyethylenes have a remarkably high degree of crystallinity in comparison with high-pressure polyethylene, which is probably due to the difference in the nature of their short chain branching reported by Willbourn[15]; that is, according to him short chain branches of high-pressure polyethylene are ethyl and butyl branches and those of Marlex and Ziegler polyethylene are methyl, and methyl and ethyl, respectively, which are shorter than butyl. Therefore these low-pressure polyethylenes are considered to have a higher degree of crystallinity. As is mentioned already it is expected that the increasing amount of branch point of long chain branching lowers the degree of crystallinity. In this experiment, however, no appreciable result was obtained in this respect. This is probably due to the very small amount of long chain branching.

Above the melting point the values of specific volume of all samples at each temperature were equal within the experimental error. The calculation of specific volume by volume dilatometry is accompanied by a larger error as the difference between bath temperature and room temperature becomes larger. In order to reduce the error, volume-temperature measurements were performed in the temperature range from the melting point to 150°C by using a larger amount of the sample than that previously used. For this experiment the bulb (part C in Fig. 1, a) and the inside diameter of the capillary in part B were made large. As part A, the capillary of the equal diameter as previous was used, so as not to reduce the accuracy of the measurement. The amount of mercury inserted was adjusted so that its top might be at the middle part of part B at room temperature, and measurements were started after the bath temperature was raised and the top of the mercury column reached a height a little above the joint connecting parts A and B at around the melting point of the sample (Fig. 1, b). The total volume up to a height a little above the joint was measured by using mercury in advance and in the case of calculation, corrections were made in quite the same way as previously. Results thus obtained for low-pressure and high-pressure polyethylenes were almost equal and well consistent with the result shown by Gubler and Kovacs in specific volume and the degree of cubic expansion, and also with those by Danusso et al.[16] for a polyethylene and a polypropylene which has methyl branch every second carbon. From these results it was confirmed that the volume-temperature relation above melting point was equal regardless of the kind of polyethylene. These results

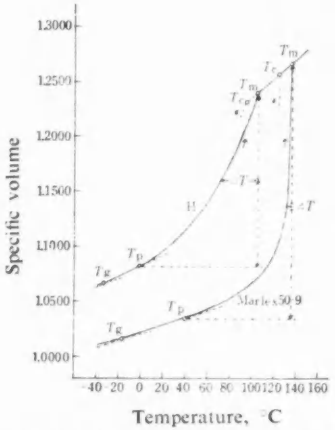

Fig. 6. Specific volume-temperature curves for Marlex 50-9 and high-pressure polyethylene H, in which the points of T_m, T_c, T_p and T_g and ΔT are shown.

15) A. H. Willbourn, *J. Polymer Sci.*, **34**, 569 (1959).

16) F. Danusso, G. Moraglio and G. Natta, *Ind. Plastiques Mod. (Paris)*, **10**, 40 (1958).

TABLE II. TEMPERATURES OF VARIOUS TRANSITIONS OF POLYETHYLENES IN °C

Sample	N_c	T_m	T_c	T_p	T_g	ΔT
Marlex 50-9	0.25	135.5	125.0	40.5	−16.0	2.5
Ziegler	0.4	132.1	122.0	30.8	−19.0	6.1
G	0.6	122.8	113.7	21.5	−22.2	11.8
A	1.6	113.2	106.8	13.3	−25.2	19.3
B	1.6	113.5	108.5	10.9	−25.8	21.0
E	1.6	113.5	105.6	11.7	−26.3	19.8
F	2.0	111.6	102.9	4.5	−27.3	22.1
C	2.2	109.8	103.2	5.5	−28.8	22.8
D	3.0	108.1	100.8	−1.8	−32.5	30.7
H	3.2	105.1	94.1	−2.0	−34.0	32.1

led to the following equation by using the method of least square;

$$V_{sp}=9\times10^{-4}T+1.1480$$

As is shown in Fig. 6 for Marlex 50-9 and high-pressure polyethylene H as examples, the specific volume-temperature curve of polyethylene has several transition points peculiar to the kind of polyethylene, that is, a melting point T_m, a crystallizing point T_c, a glass transition temperature T_g, and a premelting point T_p, at which the volume-temperature relation above T_g deviates from the straight line and polyethylene crystals are considered to begin to melt. Their temperatures became higher with the decrease of degree of short chain branching. They are listed in Table II in the order of degree of short chain branching. The curvature of the curve between premelting point and melting point which showed the premelting process grew larger and the curve came to show almost typical first order transition as the amount of short chain branching became smaller. The premelting phenomenon is considered to be due to the variety of the size of crystalline regions in polyethylene which have different melting points according to their size. According to Gubler and Kovacs the crystalline region of low-pressure polyethylene is on the whole considerably larger than that of high-pressure polyethylene. Therefore it is considered that low-pressure polyethylene begins and finishes melting at the higher temperature and sharply at that. In order to show quantitatively the difference of curvature of these curves, ΔT was given in Table II for each sample. Here, ΔT represents the temperature difference beween the melting point and the point at which half of the difference between specific volume at the premelting point and that at the melting point is shown (Fig. 6). The values of ΔT were plotted as a function of short chain branching in Fig. 7. Among high-pressure polyethylenes it seems that these values increase with the increasing amount of short chain branching and between these two quantities

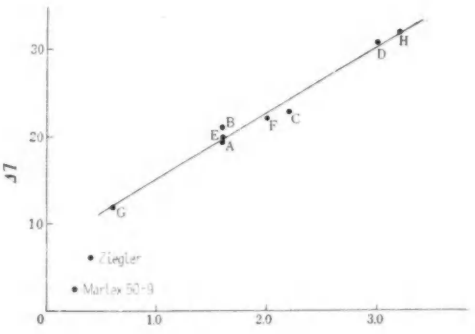

Fig. 7. The relation between short chain branching and the temperature difference between T_m and the point where half of the difference in specific volumes at T_p and T_m are shown.

the following linear relationship is obtained approximately;

$$\Delta T=7.7N_c+7.3$$

According to Hunter and Oakes, melting point, crystallizing temperature and premelting phenomenon were dependent upon the molecular weight of the sample. In this experiment the values of T_m, T_c, T_p and T_g apparently rose with the increase of molecular weight on the whole. But sample E showed almost equal values of these temperatures to those of samples A and B, though it had lower molecular weight by about 10,000 than samples A and B, and it was the same with samples C and F, that is, sample F which is almost equal in the amount of short chain branching to sample C and in molecular weight more than double that of sample C, showed almost equal values of these temperatures to those of sample C. Therefore it seems that molecular weight has almost no or a very small effect on these temperatures in comparison with short chain branching.

The glass transition temperature appears at

present to be considered -21°C regardless of molecular weight, degree of crystallinity and degree of chain branching from the experimental results by Danusso et al., though there had been presented different values by other researchers previously. The results obtained in this experiment, however, showed that the glass transition temperature of polyethylene was dependent upon the degree of short chain branching. The details about this will be presented later.

As quenched polyethylene has a very low degree of crystallinity and crystalline regions of rather small size are considered to be distributed in it, it is expected that quenched low-branched polyethylene melts in the process similar to that of highly-branched polyethylene. Therefore volume temperature measurements were carried out by using quenched Marlex 50-9. Quenching of the sample was performed by immersing the dilatometer containing the sample and mercury into the toluene-bath cooled at -40°C after it was kept at 150°C for about three hours. The volume-temperature curve for Marlex 50-9 treated in this way is shown in Fig. 8 with the curve for the most highly crystallized Marlex 50-9. This quenched sample had a low degree of crystallinity of 38.6% at 25°C. The result as expected, however, was not obtained, but the curve showing sharp melting phenomenon was obtained, which is probably due to further crystallization which is occurring slowly on raising temperature. Similar measurements were performed by using sample H quenched in the same way. The volume-temperature curve was also illustrated in Fig. 8 with the curve for the most highly crystallized sample H. The degree of crystallinity of this quenched sample was 40.0% at 25°C. The curve for quenched and the most highly crystallized Marlex 50-9 do not overlap with each other up to just below melting point, while the curve for quenched sample H falls on the curve for the most highly crystallized sample at around 50°C. From these results it is considered that further crystallization of the quenched sample occurs at a lower temperature and more easily in highly-branched polyethylene than in low-branched polyethylene. Probably short chain branchings of polyethylene expand the average intermolecular distances in the amorphous regions and weaken the intermolecular interaction, and as a result the molecules can begin to move easily at low temperature.

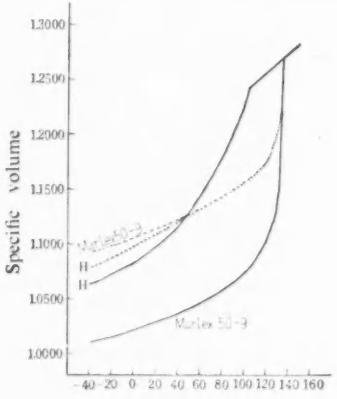

Fig. 8. Volume-temperature curves of Marlex 50-9 and high-pressure polyethylene H obtained for the most highly crystallized and quenched samples.

Summary

The specific volumes of various kinds of polyethylenes with the different degrees of short chain and long chain branchings were measured by volume dilatometry in the temperature range from -40° to 150°C, and volume-temperature curves were determined. Polyethylene having the higher degree of short chain branching had the higher specific volume at any temperature below the melting point. Above the melting point specific volumes of all the polyethylenes were equal at the same temperature. Melting point, crystallizing temperature, premelting point, and glass transition temperature were raised with the decrease of degree of short chain branching. The curvature of the curve showing premelting process grew large as the amount of short chain branching contained in the sample became small, and came to show the typical first order transition phenomenon.

The author is indebted to Professor Masatami Takeda for his helpful suggestions and discussion. He also thanks Dr. C. F. Hammer of E. I. du Pont de Nemours and Company for providing the samples of polyethylene. It is also a pleasure to aknowledge the assistance in experimental work given by Miss Masako Yoshida.

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*Stability of Complexes of Several Carboxylic Acids Formed with Bivalent Metals**

By Motoo YASUDA, Kazuo YAMASAKI and Hitoshi OHTAKI**

(Received February 4, 1960)

Numerous reports have been published on the stability of various complexes formed between bivalent metals and carboxylic acids; however, no extensive study regarding these complexes has ever been performed in any one laboratory under identical experimental conditions. Experiments under identical conditions are of primary importance because the respective values of the stability of these complexes and the differences between these values are quite small; therefore, a precise comparison of these stability constants is possible only when the values determined under the same conditions are available.

In this report the stability of various complexes formed between carboxylic acids and bivalent metals having the ratio of 1 : 1 was determined by using the pH titration method. The monobasic and dibasic acids containing the COOH groups alone were studied, i. e. the acids containing the OH groups in addition to the COOH group were excluded. Thus tartaric acid or similar acids were not studied because of their rather complicated bahavior in a solution.

Experimental

Materials.—The nitrates of lead, copper, cadmium, zinc and nickel were chemicals of the analytical grade. The carboxylic acids used are listed in Table I. They were reagents of the analytical or highest grade available.

Procedure.—The pH values were measured with a pH meter having a glass electrode made by Horiba and Co. The temperature of the measurement was 25°C and the ionic strength of the solution was maintained at 0.1 by the addition of sodium perchlorate; however, in some cases where the stability of the complex was small such as in the nickel benzoate complex the ionic strength of the solution was kept at 0.1 by nickel nitrate itself without the addition of sodium perchlorate.

The concentration of the metal nitrate was kept generally higher than that of the carboxylic acid to prevent the formation of a complex having the metal to ligand ratio of 1 : 2. The concentrations used were as follows:

Monobasic acids

Lead nitrate	0.004~0.02M	Acid	0.004~0.009M
Copper nitrate	0.006~0.015	〃	0.004~0.009
Cadmium nitrate	0.03	〃	0.012
Zinc nitrate	0.034	〃	0.012
Nickel nitrate	0.026	〃	0.009~0.012

Dibasic acids except diglycolic and thiodiglycolic acids

Lead nitrate	0.004M	Acid	0.002M
Copper nitrate	0.003	〃	0.002
Cadmium nitrate	0.006	〃	0.01
Zinc nitrate	0.007	〃	0.01
Nickel nitrate	0.01	〃	0.01

Diglycolic and thiodiglycolic acids

Lead nitrate	0.002M	Acid	0.001M
Cadmium nitrate	0.002	〃	0.001
Zinc nitrate	0.002	〃	0.001
Copper nitrate	0.0015	〃	0.001
Nickel nitrate	0.0026	〃	0.001

To convert the hydrogen ion activity into its concentration in the solution, the value 0.83 suggested by Kielland[1] was used.

Results

Acid Dissociation Constant.—If the dibasic acid is represented as H_2A, the acid dissociation constants to be determined may be expressed as

$$K_1 = \frac{[H^+]\,[HA^-]}{[H_2A]} \qquad (1)$$

and

$$K_2 = \frac{[H^+]\,[A^{2-}]}{[HA^-]} \qquad (2)$$

where [ ] expresses the concentration in mole per litre. The values of the dissociation constant were determined by titration with alkali and they are given in Table I[2]. For some dicarboxylic acids such as succinic, itaconic, glutaric, adipic, diglycolic and thiodiglycolic acids the first and second dissociation occurred simultaneously and the method of successive approximation was used to calculate their dissociation constants.

Stability Constant.—The values of the stability constant of the complexes formed are expressed by

* Presented at the XVIIth International Congress of Pure and Applied Chemistry held at Munich in 1959.

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1) J. Kielland, *J. Am. Chem. Soc.*, **59**, 1675 (1937).

2) The results for phthalic acid were taken from the report by M. Yasuda, K. Suzuki and K. Yamasaki, *J. Phys. Chem.*, **60**, 1649 (1956).

TABLE I. ACID DISSOCIATION CONSTANTS
25°C, $\mu = 0.1$

	Acids	pK_1	pK_2
1	Acetic acid	4.53	
2	Benzoic acid	4.01	
3	*o*-Methoxybenzoic acid	3.90	
4	Succinic acid	4.00	5.21
5	Itaconic acid	3.68	5.14
6	Glutaric acid	4.14	5.01
7	Adipic acid	4.28	5.00
8	Phthalic acid	2.76	4.92
9	Malonic acid	2.76	5.29
10	Maleic acid	~2	5.79
11	Citraconic acid	2.2	5.60
12	Diglycolic acid	2.77	3.92
13	Thiodiglycoic acid	3.15	4.13

$$k_1 = \frac{[MA]}{[M^{2+}]\,[A^{2-}]} \tag{3}$$

Under the conditions in the present experiments, the formation of complexes having a metal to ligand ratio of 1:2 is negligible. Therefore the species present in the solutions are H^+, M^{2+}, MA, A^{2-}, HA^-, H_2A and OH^- except in the case of sodium and perchlorate ions which were added in order to keep the ionic strength of the solution constant. Then the following relations exist between the total concentrations of acidic hydrogen, acid and metal for which the symbols C_H, C_A and C_M are used respectively.

The concentration of OH^- is negligible in acid solutions.

Thus

$$C_H = [H^+] + [HA^-] + 2[H_2A] \tag{4}$$

$$C_A = [A^{2-}] + [HA^-] + [H_2A] + [MA] \tag{5}$$

$$C_M = [M^{2+}] + [MA] \tag{6}$$

By substituting Eqs. 1 and 2 into 4, Eq. 7 may be obtained

$$C_H - [H^+] = \frac{[H^+]\,[A^{2-}]}{K_2} + \frac{2[H^+]^2[A^{2-}]}{K_1K_2} \tag{7}$$

From the pH measurements of the solutions $[H^+]$ was calculated. By substituting $[H^+]$ into 7 $[A^{2-}]$ was found and then [MA] and $[M^{2+}]$ were obtained from 5 and 6 combined with 1 and 2 and finally $k_1 = [MA]/[M^{2+}]\,[A^{2-}]$ was found. The logarithmic values of the stability constant thus obtained are given in Table II. For monobasic acids the calculations are more simple than for dibasic acids shown above.

The stability of these complexes under somewhat different experimental conditions of temperature and ionic strength have been previously determined by several other authors, as listed in Table III:

If the differences in temperature and ionic strength of the solution are taken into consideration, their results agree fairly well with the results of the present study.

From the results shown in Table II the acids studied are divided into three groups:

1) Dibasic acids forming a seven membered or a larger chelate ring and having no double bonds in the chelate ring. Monobasic acids also belong to this group.

2) Dibasic acids forming a six membered ring such as malonic acid and those having double bonds in the chelate ring such as maleic and citraconic acids.

3) Dibasic acids seeming to act as tridentate chelating agent. Diglycolic and thiodiglycolic acids belong to this group.

It is obvious from Table II that the acids of the first group form complexes whose stability constants follow the order

$$Pb > Cu > Cd > Zn > Ni$$

and that lead shows the highest stability. The values for monobasic acids are nearly

TABLE II. STABILITY CONSTANTS ($\log k_1$)

	Acids	Pb	Cu	Cd	Zn	Ni
1	Acetic acid	2.1	1.8	1.5	1.0	1.0
2	Benzoic acid	2.0	1.6	1.4	0.9	0.9
3	*o*-Methoxybenzoic acid	1.9	1.6	1.3	0.9	0.8
4	Succinic acid	2.8	2.6	2.1	1.6	1.6
5	Itaconic acid	3.1	2.8	2.3	1.9	1.8
6	Glutaric acid	2.8	2.4	2.0	1.6	1.6
7	Adipic acid	2.8	2.3	2.1	1.8	1.6
8	Phthalic acid[4]	ppt.	3.1	2.5	2.2	2.1
9	Malonic acid	3.1	5.0	2.3	2.7	3.2
10	Maleic acid	3.2	3.4	2.4	2.0	2.0
11	Citraconic acid	3.3	3.4	2.2	1.8	1.8
12	Diglycolic acid	4.4	3.9	3.3	3.6	2.6
13	Thiodiglycolic acid	3.6	4.3	2.6	2.9	4.0

TABLE III

Acids	References
Acetic	Cannan and Kibrick[3]
	Lloyd, Wycherley and Monk[4]
	Edmonds and Birnbaum[5]
	Fronaeus[6]
	Tanaka et al.[7]
Succinic	Cannan and Kibrick[3]
	Peacock and James[8]
Glutaric	Cannan and Kibrick[3]
	Peacock and James[8]
Adipic, phthalic and maleic	Peacock and James[8]
Malonic	Riley[9]
	Stock and Davies[10]
	Money and Davies[11]
Diglycolic and thiodiglycolic	Tichane and Bennett[12]

the same and show only small differences between them. The dibasic acids show higher values than monobasic acids. Both succinic and itaconic acids form seven membered rings, but the stability constants are a little larger for the latter, which has a double bond in the side chain.

The empirical stability order for bivalent metals was proposed by various authors and the order

$$Cu > Ni > Pb > Co,\ Zn$$

found by Mellor and Maley[13] holds with some variations for many O and N type ligands. Irving and Williams[14] pointed out that the order

$$Zn < Cu > Ni > Co > Fe > Mn$$

for the metals of the first transition series held irrespective of the nature of the ligands involved. However, generally the order of stability depends on the nature of ligands, especially when metals of non-transition series are concerned.

The stability constants of more than five hundred ligands have so far been determined, but no example of a ligand showing a high stability for lead has been found except in the case of β-(*S*-ethyl)mercaptopropionic acid as determined by Irving and Fernelius[15] in a water-dioxane mixture. The order of stability found by them is the same as the present one, i. e. lead showed the highest stability. The highest stability found in the lead complexes of carboxylic acids is, therefore, quite remarkable. The exact reason for the large stability of lead is rather difficult to explain at present.

The above mentioned order in the first group does not hold for the acids in the second group. The complexes of malonic acid which form six membered chelate rings follow the stability order

$$Cu > Ni > Pb > Zn > Cd$$

However, with the other two acids, maleic and citraconic acids which form seven membered chelate rings, copper is the highest in the stability order,

$$Cu > Pb > Cd > Zn > Ni$$

Citraconic acid has a methyl group and its effect seems to decrease somewhat the stability, perhaps due to steric hindrance.

If the size of the chelate ring for one metal is compared, for example, for copper, the stability is highest for malonic acid and it decreases in the following order as the size of the chelate ring increases,

malonic acid	six membered ring,
succinic acid	seven membered ring,
glutaric acid	eight membered ring,
adipic acid	nine membered ring.

If we could determine the stability of oxalic acid complexes which form a five membered ring, it might be interesting. However, under the experimental conditions of the present study, precipitation occurred instantaneously. The stability of oxalic acid complexes given in the literature are few and no data for lead are available.

For the acids in the third group the order of metals are

$$Pb > Cu > Zn > Cd > Ni \quad \text{for diglycolic acid}$$

and

$$Cu > Ni > Pb > Zn > Cd \quad \text{for thiodiglycolic acid.}$$

These two acids have rather small values for their acid dissociation constants. On the other hand, the values of their stability constant are large and it seems that they form tridentate complexes with O and S atoms participating in the chelation as Tichane and Bennett[12] pointed out.

3) R. K. Cannan and A. Kibrick, *J. Am. Chem. Soc.*, **60**, 2314 (1938).
4) M. Lloyd, V. Wycherley and C. B. Monk, *J. Chem. Soc.*, **1951**, 1786.
5) S. M. Edmonds and N. Birnbaum, *J. Am. Chem. Soc.*, **62**, 2367 (1940).
6) S. Fronaeus, *Acta Chem. Scand.*, **6**, 1200 (1952).
7) N. Tanaka et al., This Bulletin, **32**, 516 (1959); **33**, 417 (1960).
8) J. M. Peacock and J. C. James, *J. Chem. Soc.*, **1951**, 2233.
9) H. L. Riley, ibid., **1930**, 1642.
10) D. I. Stock and C. W. Davies, ibid., **1949**, 1371.
11) R. W. Money and C. W. Davies, *Trans. Faraday Soc.*, **28**, 609 (1932).
12) R. M. Tichane and W. E. Bennett, *J. Am. Chem. Soc.*, **79**, 1293 (1957).
13) L. E. Maley and D. P. Mellor, *Austhal. J. Sci. Res.*, **A2**, 92, 579 (1949).
14) H. Irving and R. J. P. Williams, *J. Chem. Soc.*, **1953**, 3192.
15) R. J. Irving and W. C. Fernelius, *J. Phys. Chem.*, **60**, 1427 (1956).

In connection with this point, *o*-methoxybenzoic acid was studied to ascertain whether the O atom of the methoxy group participates in the chelation. The values for *o*-methoxybenzoic acid complexes were nearly the same as those of the benzoic acid complexes. This appears to mean that the O atom of the methoxy group has very little relation to the chelation.

Concerning the chelating tendency of various bivalent metals for O and S atoms of similar ligands, several studies have been made on *o*-aminobenzenethiol[16], β-mercaptopropionic acid[17], β-(*S*-ethyl)mercaptopropionic acid[15] and purine derivatives[18], and zinc was found to form a stronger complex than nickel when sulfur is involved in the metal-ligand bond. However, this is not the case for thiodiglycolic acid, and a more detailed study on ligands containing sulfur is desirable to elucidate this problem.

Finally the use of these dicarboxylic acids as the eluting agent of the metal ions adsorbed on ion exchange resins was investigated. As the acid, adipic acid was chosen, as it showed suitable differences of stability for various metals.

Metal ions were adsorbed on the resin Dowex 50, H-form. Sodium adipate solution of pH 5.2 (0.1 molar solution) was poured into the column. Lead was omitted as it formed a precipitate in the 0.1 molar solution of sodium adipate. The metals in the eluted solution were determined by titration with ethylenediaminetetraacetate. The vertical axis of the graph (Fig. 1) indicates the values proportional to the metal concentration in each fraction (5 ml.) and the horizontal axis the fraction number. The separation between copper, cadmium and zinc is complete, but the separation between zinc and nickel is not. Diglycolic acid was also tested for the eluting agent, but in this case the tailing of each metal was remarkable and the complete separation was difficult.

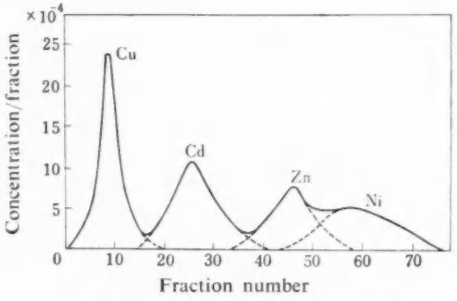

Fig. 1. Elution of Cu, Cd, Zn and Ni ions by adipic acid.

Resin: Dowex 50×−4
Column: dia. 1 cm.×5 cm.
Flow rate: 0.5 ml. per min.
Adipic acid: 0.1 M pH 5.2
One fraction: 5 ml.

Summary

Stability constants of the bivalent metal complexes formed with several mono- and dicarboxylic acids were determined at 25°C and ionic strength of 0.1. For monocarboxylic acids and several dicarboxylic acids having no double bond or forming larger chelate rings than six membered rings the following stability order held: Pb>Cu>Cd>Zn>Ni. It is very remarkable that lead showed the highest stability among bivalent metals.

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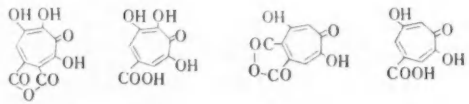
16) R. G. Charles and H. Freiser, *J. Am. Chem. Soc.*, **74**, 1385 (1952).
17) Q. Fernando and H. Freiser, ibid., **80**, 4928 (1958).
18) G. E. Cheney, H. Freiser and Q. Fernando, ibid., **81**, 2611 (1959).

Synthesis of Puberulonic Acid[1]

By Tetsuo Nozoe, Kozo Doi* and Tokuro Hashimoto**

(Received January 16, 1960)

Puberulonic acid (I) was first isolated, together with puberulic acid (II), by Birkinshaw and Raistrick[2] from cultures of the moulds *Penicillium puberulum* Bainer and *P. aurentiovirens* Biourge. These mould tropolones (I and II) have been reported to have a significant antibiotic activity against various Gram-positive organisms[3]. The structure I for puberulonic acid has been accepted reasonably by the presence of a dicarboxylic anhydride grouping evidenced from the data of the infrared spectrum[4], ultraviolet spectrum[5] and titration[6], and by the decarboxylation of it to puberulic acid[6,7] (II). As other mould tropolones, stipitatonic acid[8] (III) and stipitatic acid[9] (IV) have been isolated from culture of *P. stipitatum* Thom. Of the above four mould tropolones, puberulic acid[10] (II) and stipitatic acid[11,12] (IV) have already been synthesized by Johnson and his collaborators from 1, 2, 4-trimethoxybenzene and diazoacetate.



I II III IV

The present authors have been able to synthesize puberulonic acid (I), the details of which will be reported in this communication.

The starting material used was tropolone-3, 4-dicarboxylic anhydride[13] (V), which had been obtained in a poor yield by alkaline hydrogen peroxide oxidation[14] of purpurogallin, of which synthesis[15] had been completed by Haworth and his co-workers. The structure of the anhydride V had been proved by the conversion of it to benzene-1, 2, 3-tricarboxylic acid with alkali-fusion.

As an approach to the synthesis of puberulonic acid (I), it was adopted, that an introduction of bromine, followed by replacing of the bromine with the hydroxyl group, into the anhydride V, was carried out and that a further brominationhydroxylation process were repeated in the resulted hydroxytropolone-dicarboxylic anhydride (XIII). To the reaction for replacing bromine atom with the hydroxyl group, the Rosenmund method[16], in which *o*-bromobenzoic acid was converted into salicylic acid, was satisfactorily applied.

When 3-bromotropolone (VI) was heated with sodium β-naphthalenesulfonate in dilute alkaline solution, 3-hydroxytropolone (VII) was obtained in a 40% yield. This fact proves that a normal nucleophilic substitution of the bromine into the hydroxyl group took place in the above reaction, contrary to formation of 4-hydroxytropolone, a *ciné* (abnormal) substitution product, in high temperature hydrolysis of 3-bromotropolone (VI) with 75% potassium hydroxide[17]. Application of similar reaction to 3, 7-dibromotropolone (VIII) afforded in less yield 3, 4-dihydroxytropolone (IX), which was proved to be identical with the compound known as "decarboxylated puberulic acid"[6,18].

Bromination of tropolone-3, 4-dicarboxylic anhydride (V) in acetic acid gave easily 7-bromotropolone-3, 4-dicarboxylic anhydride (X) in a good yield. Heating of the anhydride X in

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1) This article was read at the 11th Annual Meeting of the Chemical Society of Japan, April, 1957; partly read by T. Nozoe at the 16th International Congress of IUPAC in Paris, July 18, 1957.

2) J. H. Birkinshaw and H. Raistrick, *Biochem. J.*, **26**, 441 (1932).

3) A. E. Oxford, H. Raistrick and G. Smith, *Chem. & Ind.*, **61**, 485 (1942).

4) A. W. Johnson, N. Sheppard and A. R. Todd, *J. Chem. Soc.*, **1951**, 1139.

5) G. Aulin-Erdtman, *Acta Chem. Scand.*, **4**, 1325 (1950); **5**, 301 (1951).

6) R. E. Corbett, C. Hassal, A. W. Johnson and A. R. Todd, *J. Chem. Soc.*, **1950**, 1.

7) R. E. Corbett, A. W. Johnson and A. R. Todd, ibid., **1950**, 6.

8) a) W. Segal, *Chem. & Ind.*, **1957**, 1040. b) K. Doi and Y. Kitahara have corrected the earlier formulation of stipitatonic acid by W. Segal to that of III. This Bulletin, **31**, 788 (1958).

9) J. H. Birkinshaw, A. R. Chambers and H. Raistrick, *Biochem. J.*, **36**, 242 (1942).

10) R. B. Johns, A. W. Johnson and J. Murray, *J. Chem. Soc.*, **1954**, 198.

11) J. R. Bartels-Keith, A. W. Johnson and W. I. Taylor, ibid., **1951**, 2352.

12) R. B. Johns, A. W. Johnson and M. Tisler, ibid., **1954**, 4605.

13) T. Nozoe et al., *Science Repts. Tohoku Univ., Ser.* I, **38**, 257 (1954).

14) W. D. Crow, R. D. Haworth and P. R. Jefferies, *J. Chem. Soc.*, **1952**, 3705.

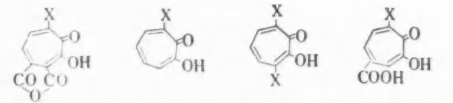
15) D. Caunt, W. D. Crow, R. D. Haworth and C. A. Vodoz, ibid., **1950**, 1631.

16) K. W. Rosenmund and H. Harms, *Ber.*, **53**, 2226 (1920).

17) Y. Kitahara, *Science Repts. Tohoku Univ., Ser.* I, **39**, 258 (1956).

18) G. Barger and O. Dorrer, *Biochem. J.*, **28**, 11 (1934).

water at 180°C afforded 3-bromo-6-carboxytropolone[19] (XI), a bromination product of 4-carboxytropolone (XII). This fact, together with derivation of 3-hydroxytropolone (VII) from the compound XIII described below, appears to determine the position of the bromine-atom in the molecule X.

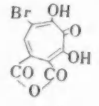


V: X=H VI: X=Br VIII: X=Br XI: X=Br
X: X=Br VII: X=OH IX: X=OH XII: X=H
XIII: X=OH XIV: X=OH

Reaction of the bromo derivative X with sodium β-naphthalenesulfonate in weak alkaline solution for four hours gave 3-hydroxytropolone-4, 5-dicarboxylic anhydride (XIII) in a good yield. The replacement of the bromine-atom in the compound X with hydroxyl group appeared to be more facile than in the cases of 3-bromotropolone (VI) and 3, 7-dibromotropolone (IX), the fact of which indicates probably, that the bromine-atom in the former X is activated by the dicarboxylic anhydride grouping situated at the *p*-position.

It was found, that stipitatonic acid[8a] (III) gives stipitatic acid (IV) under the same condition as that[3] of formation of puberulic acid (II) from puberulonic acid (I). On the contrary, 3-hydroxytropolone derivative XIII did not decarboxylate under the same condition, but caused decarboxylation under heating with water in a sealed tube at 180°C to 5-carboxy-3-hydroxytropolone (XIV), which corresponds to "isostipitatic acid"[10,12], synthesized already by Johnson and others. Subsequent heating of the compound (XIV) at its melting point gave 3-hydroxytropolone (VII). 3-Hydroxytropolone-4, 5-dicarboxylic anhydride (XIII) was also obtained by treatment of the corresponding bromo derivative X with 75% potassium hydroxide or by persulfate oxidation of the anhydride V, the details of which will be reported elsewhere.

It was found, that the monobromination of the hydroxy compound XIII was unexpectedly difficult. Addition of bromine to XIII in acetic acid appeared to result in consumption of about one-half of the calculated amount of bromine, and the successive isolation procedure of the product left only charred matter. This fact recalls an observation of Johnson and others on bromination of isostipitatic acid[10] (XIV). In this series of experiments, however, 7-bromo-3-hydroxytropolone-4, 5-dicarboxylic anhydride (XV) could be obtained by the bromination of XIII in the presence of sodium hydrogen sulfite in a 50% yield.



XV

Fig. 1 shows the ultraviolet absorption spectra of the foregoing four intermediates (V, X, XIII and XV). The absorption maximum near 350 mμ in curves (1) and (2) is respectively split into three absorption peaks in curves (3) and (4), the fact of which is probably characteristic of those of 3-hydroxytropolones[20].

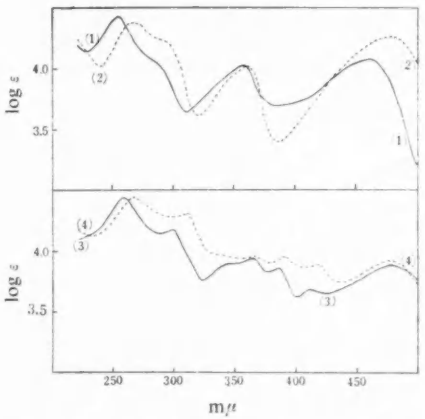


Fig. 1. Ultraviolet absorption spectra in methanol.
(1): Tropolone-3, 4-dicarboxylic anhydride (V)
(2): 7-Bromotropolone-3, 4-dicarboxylic anhydride (X)
(3): 3-Hydroxytropolone-4, 5-dicarboxylic anhydride (XIII)
(4): 7-Bromo-3-hydroxytropolone-4, 5-dicarboxylic anhydride (XV)

Treatment of the bromo derivative XV with sodium β-naphthalenesulfonate in slightly alkaline solution resulted in formation of puberulonic acid (I) in a 35% yield. The nucleophilic reactivity of the bromine atom in XV seemed to be distinctly smaller than that of the bromine in X. Puberulonic acid (I) synthesized as above did not show any depression of the melting point on admixture with a natural one[21].

19) Y. Kitahara, *Science Repts. Tohoku Univ., Ser.* I, **40**, 74 (1956).

20) T. Nozoe et al., ibid., **37**, 191 (1953); **40**, 121 (1957).

21) It was separated from a mixture of puberulonic and puberulic acids, m. p. 275°C (decomp.), which Professor J. H. Birkinshaw had kindly sent to us.

Puberulic acid (II), obtained by decarboxylation of the synthesized puberulonic acid, also showed no depression of the melting point on admixture with a natural one[21].

In Fig. 2 are shown the comparisons of the ultraviolet absorption spectra of synthetic puberulonic and puberulic acids with natural ones, and in Table I is shown, that of the infrared absorptions (6 μ bands) of synthetic and natural puberulonic acid.

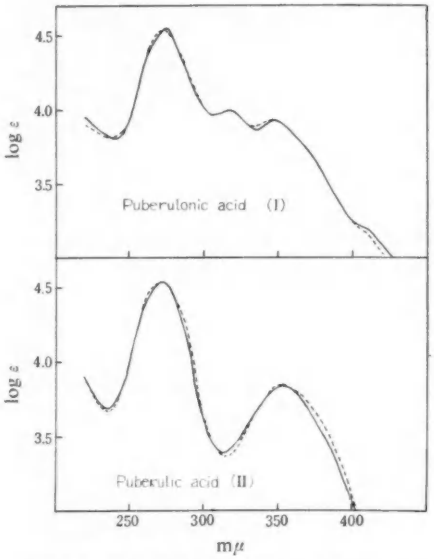


Fig. 2. Ultraviolet absorption spectra in water.
(——): Synthetic products
(------): Natural products

TABLE I. COMPARISON OF THE INFRARED ABSORPTION OF SYNTHETIC AND NATURAL PUBERULONIC ACID

Puberulonic acid	M.p.	Main strong bands cm^{-1}				
Synthetic[22]	293°C	1830	1765	1618	1545	KBr
Natural[22]	293°C	1830	1765	1618	1545	KBr
Johnson et al.[4]	298°C	1830	1770	1615	1544	Nujol

Experimental[23]

3-Hydroxytropolone (VII).—A mixture of 3-bromotropolone (VI, 0.60 g.), sodium β-naphthalenesulfonate (0.76 g.), sodium hydroxide (0.4 g.), copper bronze (60 mg.) and water (45 cc.) was heated under reflux for 4 hr. The filtrate, from which copper was removed, was acidified with dilute sulfuric acid to Congo-red and extracted with ethyl acetate (100 cc.). The evaporated residue of the extract, after sublimation in vacuo followed by crystallization from cyclohexane, gave 3-hydroxytropolone (VII, 0.14 g., 44%), m. p. 136°C, undepressed on admixture with an authentic specimen[20].

3, 4-Dihydroxytropolone (IX).—A mixture of 3,7-dibromotropolone (VIII, 0.28 g.), sodium β-naphthalenesulfonate (0.7 g.), sodium hydroxide (0.2 g.), copper powder (10 mg.) and water (30 cc.) was heated under reflux for 8 hr. The similar procedure as above described, after sublimation in vacuo and subsequent crystallization from ethyl acetate, yielded 3, 4-dihydroxytropolone (IX, 35 mg., 22%), colorless prisms, m. p. 237°C (reported 233~235°C[19], 237~238°C[6]).

Found: C, 54.58; H, 4.00. Calcd. for $C_7H_6O_4$: C, 54.55; H, 3.92%.

The ultraviolet absorption, having maxima at 272 mμ (log ε 4.64) and 355 (3.95) in water, was identical with that of the reported decarboxylated puberulic acid[6].

7-Bromotropolone-3, 4-dicarboxylic Anhydride (X).—To a stirred mixture of the dicarboxylic anhydride (V, 2.5 g.), sodium acetate trihydrate (1.8 g.) and acetic acid (40 cc.) was added, dropwise, bromine (2.1 g.) in acetic acid (5 cc.). After being stirred for 2 hr. at room temperature, the mixture was diluted with water, acidified with dilute sulfuric acid to Congo-red, and then extracted with methyl ethyl ketone. The concentrated residue of the extract was crystallized from acetic acid to form 7-bromotropolone-3,4-dicarboxylic anhydride (X, 3.0 g., 86%), yellow needles, m. p. 197~198°C. The analytical sample, m. p. 198°C, was obtained after sublimation in vacuo following recrystallization from acetic acid.

Found: C, 39.73; H, 1.42. Calcd. for $C_9H_3O_5Br$: C, 39.85; H, 1.11%.

λ_{max}^{MeOH} mμ (log ε): 265 (4.38), 362 (4.03), 480 (4.27).

Decarboxylation of X.—A mixture of the bromotropolonedicarboxylic anhydride (X, 70 mg.) and water (3 cc.) was heated in a sealed tube at 180°C for 2 hr. The evaporated residue, after sublimation in vacuo and successive crystallization from methanol, afforded 3-bromo-6-carboxytropolone (XI, 20 mg.), pale yellow prisms, m. p. 233~234°C, alone or mixed on admixture with an authentic specimen[17].

3-Hydroxytropolone-4, 5-dicarboxylic Anhydride (XIII).—A mixture of the bromo derivative (X, 0.5 g.), sodium β-naphthalenesulfonate (0.42 g.), sodium hydroxide (0.3 g.), copper powder (10 mg.) and water (6 cc.) was heated on a boiling water bath for 4 hr. The filtrate, after copper was removed from the mixture, was acidified with dilute sulfuric acid to Congo-red and extracted with ether for 48 hr. continuously. The evaporated residue of the extract, after being washed with a small volume of methanol, gave 3-hydroxytropolone-4,5-dicarboxylic anhydride (XIII), yellow prisms, m. p. 254~255°C. Yield, 0.32 g. (83%). The analytical sample melted at 258°C was obtained by sublimation in vacuo and by successive recrystallization from acetic acid.

22) The infrared spectra were measured by a Perkin-Elmer Model 21 Infrared Spectrometer with a rock salt prism.
23) All melting points are uncorrected.

Found: C, 51.74; H, 2.02. Calcd. for $C_9H_6O_6$: C, 51.93; H, 1.94%.

λ_{max}^{MeOH} mμ (log ε): 258 (4.44), 300 (4.14), 365 (3.94), 385 (3.88), 410 (3.69), 475 (3.90).

Decarboxylation of XIII.—A mixture of XIII (100 mg.) and water (4 cc.) was heated in a sealed tube at 180°C for 2 hr. The reaction mixture was evaporated and the residual solid was washed with ethyl acetate. The soluble part in the same solvent afforded 3-hydroxytropolone (VII, 15 mg.), undepressed on admixture with an authentic specimen[20]. The less soluble part, after crystallization from water, gave 5-carboxy-3-hydroxytropolone (XIV, 40 mg.), m. p. 279°C (decomp.), of which further heating at its decomposition point yielded 3-hydroxytropolone. The product XIV is assumed to correspond to impure "isostipitatic acid"[10,12], having m. p. of 282°C.

7-Bromo-3-hydroxytropolone-4, 5-dicarboxylic Anhydride (XV).—To astirred mixture of the hydroxytropolone-dicarboxylic anhydride (XIII, 0.21 g.), sodium acetate trihydrate (0.14 g.) and acetic acid (4 cc.), was added dropwise a solution of bromine (0.16 g.) in acetic acid (1 cc.) at room temperature. At the point of dropping of about one-half volume of bromine, sodium hydrogen sulfite (20 mg.) was added, further bromination being followed. Then, the reaction proceeded smoothly and the reaction mixture became a transparent solution, which was allowed to evaporate in vacuo over an alkali-desiccator. The residue was diluted with water, acidified with dilute sulfuric acid to Congo-red, and extracted with methyl ethyl ketone. The residue obtained after removal of the solvent crystallized from acetic acid to give the bromo derivative (XV, 0.16 g.), yellow needles, m. p. 236~237°C (decomp). The analytical sample melted at 240°C (decomp.) was obtained by sublimation in vacuo followed by recrystallization from acetic acid.

Found: C, 38.00; H, 1.27. Calcd. for $C_9H_3O_6Br$: C, 37.66; H, 1.05%.

λ_{max}^{MeOH} mμ (log ε): 266 (4.44), 310 (4.31), 365 (3.96), 390 (3.96), 420 (3.89), 480 (3.92).

Puberulonic Acid (I).—A mixture of the above bromo compound (XV, 0.57 g.), sodium β-naphthalenesulfonate (0.7 g.), sodium hydroxide (0.56 g.), copper powder (20 mg.) and water (7 cc.) was heated on a boiling water-bath for 8 hr. The solution obtained by removal of copper was acidified with dilute sulfuric acid to Congo-red and extracted wih ether for 48 hr. continuously. The evaporated residue of the extract crystallized to give yellow solids, m. p. 265~270°C (decomp.), of which washing with a small volume of methanol, sublimation in vacuo and subsequent recrystallization from methanol gave puberulonic acid (I, 15 mg., 35%), yellow crystals, m. p. 293°C (decomp.), undepressed on admixture with natural puberulonic acid[21].

Found: C, 48.04; H, 1.62. Calcd. for $C_8H_4O_7$: C, 48.23; H, 1.80%.

The ultraviolet absorption (in water) of the synthesized puberulonic acid (I) has maxima at 275 (4.54), 317 (4.00) and 447 mμ (log ε 3.94), identical with those of the authentic specimen[6].

Puberulic Acid (II).—A mixture of the above synthesized puberulonic acid (I, 80 mg.) and water (2 cc.) was heated under reflux for one hour. The evaporated residue of the mixture was dissolved in sodium hydrogen carbonate solution and treated with active charcoal. The solution obtained by removal of the charcoal crystallized by acidification with dilute sulfuric acid to give puberulic acid (II, 45 mg.), colorless crystals, m. p. 317~318°C, not depressed on admixture with natural puberulic acid[21].

Found: C, 48.37; H, 2.96. Calcd. for $C_8H_6O_6$: C, 48.49; H, 3.05%.

The ultraviolet absorption spectrum (in water), having maxima at 274 (4.54) and 352 mμ (log ε 3.84), was identical with that of the authentic specimen[6]. Heating of the synthesized puberulic acid (II) at 350°C and subsequent sublimation in vacuo afforded 3,4-dihydroxytropolone (IX), undepressed on admixture with an authentic specimen.

The authors express their sincere thanks to the Ministry of Education for a monetary assistance from the Grant in Aid for Scientific Research, to Professor J. H. Birkinshaw for his kind gift of natural puberulonic and puberulic acids, to Mr. Yusaku Ikegami for the infrared spectral measurements and to Messrs. Ohyama, Kato, Iwanaga and Azumi for microanalyses.

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*Studies on Antibiotics and Related Substances. X. Syntheses of Some Unsaturated Ketocarboxylic Acids, Anti-tumor Substances**

By Mitsuhiro KINOSHITA and Sumio UMEZAWA

(Received December 26, 1959)

The anti-tumor activities of sarkomycin[1] (2-methylenecyclopentanone-3-carboxylic acid), 5-methylenecyclopentanone-3-carboxylic acid[2] and its esters prompted us to investigate some related aliphatic compounds. The present paper presents the syntheses of two isomeric methylenelevulinic acids, 4-keto-5-hexene-1-carboxylic acid and 4-keto-3-methylenepentane-1-carboxylc acid, which have been found to possess significant anti-tumor and antibacterial activities. In addition, we have described here two rare illustrations of the Mannich reaction where the formation of two isomers respecting to the methylene groups at either side of the ketone-group has been demonstrated.

δ-Methylene- and β-Methylene-levulinic Acid.—Ethyl 5-dimethylamino-3-keto-pentane-1-carboxylate hydrochloride (II) was prepared by the esterification of 5-dimethylamino-3-keto-pentane-1-carboxylic acid hydrochloride (I) which was synthesized from levulinic acid as reported by Mannich[3]. Thermal degradation of II afforded a 61% yield of ethyl δ-methylene-levulinate (III). Structural proof of II was obtained by hydrogenation of III with platinum catalyst to give a 83% yield of ethyl γ-keto-*n*-caproate (V). Mild hydrolysis of the ester III with dilute sulfuric acid afforded a crude product of δ-methylenelevulinic acid (IV), which resisted attempts to purify it. The analytically pure product of IV has been prepared by thermal degradation of 5-dimethylamino-3-keto-pentane-1-carboxylic acid hydrochloride I.

The ultraviolet absorption of III in methanol solution showed peaks at 211 and 315 mμ, suggesting the presence of an α,β-unsaturated ketone group. The absorption of IV prepared directly from I also showed peaks at 212 and 305 mμ in aqueous solution (Fig. 1). The infrared absorption characteristics of IV was just as expected, showing the presence of double bond, conjugated carbonyl and carboxyl groups

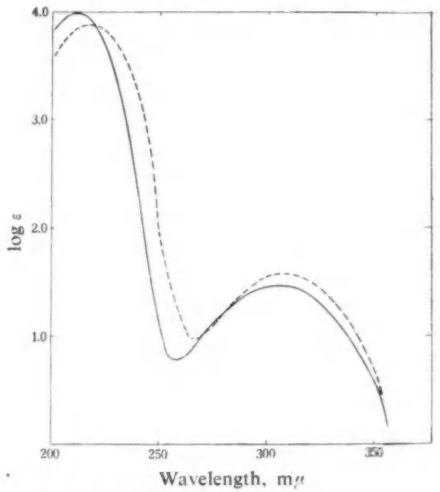

Fig. 1. Ultraviolet absorption spectra of δ-methylenelevulinic acid (——) and β-methylenelevulinic acid (----) in water.

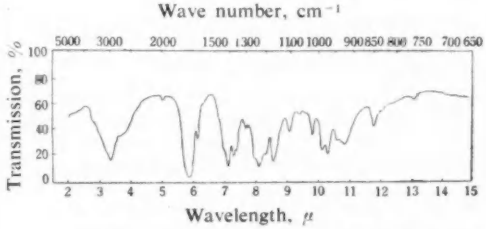

Fig. 2. Infrared absorption spectrum of δ-methylenelevulinic acid in Nujol.

(Fig. 2).

By adding a large quantity of acetone to the mother-liquor which was separated from I, the hydrochloride (VI) of 2-(dimethylaminomethyl)-3-ketobutane-1-carboxylic acid, a Mannich base isomer of I, has been obtained. Thermal degradation of VI afforded β-methylenelevulinic acid (VII), an isomer of IV. β-Methylenelevulinic acid (VII) has been found to be stable, while, δ-methylene isomer (IV) polymerized gradually on standing.

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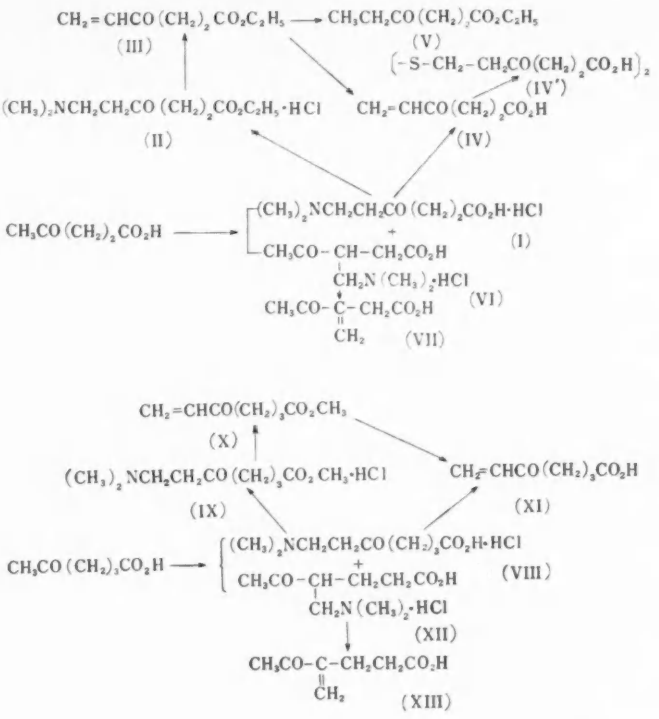
1) H. Umezawa, T. Yamamoto, T. Takeuchi, T. Osato, Y. Okami, S. Yamaoka, T. Okuda, K. Nitta, K. Yagishita, R. Utahara and S. Umezawa, *Antibiotics a. Chemotherapy*, **4**, 514 (1954).

2) S. Umezawa and M. Kinoshita, This Bulletin, **30**, 268 (1957).

3) C. Mannich and M. Bauroth, *Ber.*, **57**, 1108 (1924).



Addition of hydrogen sulfide to IV afforded ε, ε-dithio-di-γ-keto-*n*-caproic acid (IV'), which has been found to have a strongly inhibitory effect only for the growth of *Micrococcus flavus*.

4-Keto-5-hexene-1-carboxylic Acid and 4-Keto-3-methylenepentane-1-carboxylic Acid.—Methyl 4-keto-5-hexene-1-carboxylate (X) has been prepared from δ-ketocaproic acid by an analogous series of reactions as described above in the synthesis of ethyl δ-methylenelevulinate (III).

Structural proof for 6-dimethylamino-4-ketohexane-1-carboxylic acid hydrochloride (VIII) was obtained by paper chromatographic confirmation of the spot of glutaric acid as well as that of succinic acid as the oxidation products of VIII with nitric acid[3]. VIII was esterified to yield methyl ester hydrochloride IX, which was degraded by pyrolysis to yield a crude product of methyl 4-keto-5-hexene-1-carboxylate (X). Mild hydrolysis of X with dilute sulfuric acid afforded a crude product of 4-keto-5-hexene-1-carboxylic acid (XI) in a low yield, while thermal degradation of VIII gave better result, yielding XI in a 31% yield. Unexpectedly, XI was very hygroscopic and easily crystallized as its monohydrate which was stable, showing almost no tendency to polymerize.

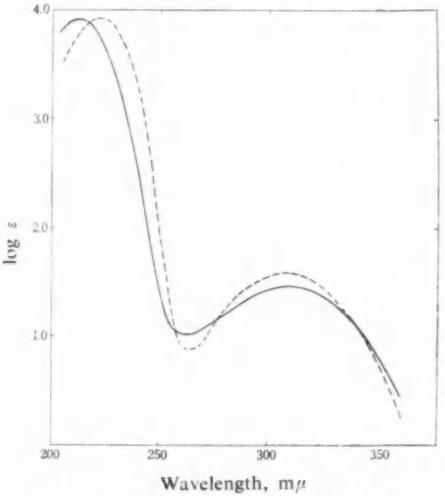


Fig. 3. Ultraviolet absorption spectra of 4-keto-5-hexene-1-carboxylic acid (——) and 4-keto-3-methylenepentane-1-carboxylic acid (----) in water.

Ozonolysis of XI gave formaldehyde as one of the products, indicating the presence of a terminal methylene group. The ultraviolet and

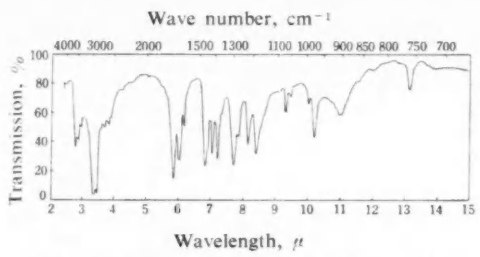


Fig. 4. Infrared absorption spectrum of 4-keto-5-hexene-1-carboxylic acid in Nujol.

infrared absorption spectra of XI presented in Fig. 3 and 4 indicated that XI is an α, β-unsaturated ketocarboxylic acid.

When the mother liquor separated from VIII was stored in a refrigerator for two weeks, the hydrochloride (XII) of 3-(dimethylaminomethyl)-4-ketopentane-1-carboxylic acid separated in a crystalline mass. The product showed a positive test for iodoform reaction, suggesting that the product still contained a terminal acetyl group. Thermal degradation of XII afforded 4-keto-3-methylenepentane-1-carboxylic acid (XIII) in 71% yield. From the fact that ozonolysis of XIII yielded formaldehyde and succinic acid in reasonable yields, the structure of XIII has been confirmed and it has been further concluded that the structure of XII is 3-(dimethylaminomethyl)-4-ketopentane-1-carboxylic acid. The ultraviolet spectrum of XIII presented in Fig. 3 indicated that XIII is an α, β-unsaturated ketocarboxylic acid.

Experimental

Separation of 5-Dimethylamino-3-ketopentane-1-carboxylic Acid Hydrochloride (I) and 2-(Dimethylaminomethyl)-3-ketobutane-1-carboxylic Acid Hydrochloride (VI) from Mannich Reaction Product.—A mixture of levulinic acid (25 g.) and dimethylamine hydrochloride (17.6 g.) was heated to 105°C in an oil bath. To the resulting melt was added paraformaldehyde (6.45 g.) and then the mixture was stirred at 105~110°C for 30 min. After evaporation under reduced pressure, the resulting syrup was dissolved in absolute ethanol (22 cc.) by warming. To the cooled solution was added acetone (93 cc.) and the mixture was allowed to stand overnight in a refrigerator to precipitate a first crystalline crop (17.5 g.); m. p. 94~104°C. Recrystallization from ethanol gave a pure sample of I (12.9 g.), m. p. 119.5~120.5°C. An additional crop (0.9 g.) of I was obtained from the recrystallization mother liquor. The total yield of I was 31%.

Acetone (135 cc.) was added to the mother liquor of the above mentioned first crop and the mixture was stored in a refrigerator for several days to give the second crystalline crop, which was collected and washed with absolute ethanol (15 cc.); yield 7.3 g., m. p. 102~115°C. Recrystallization from ethanol gave colorless short prisms of VI, yield 3.3 g., m. p. 121~122°C. By the treatment of the recrystallization mother liquor of the second crop, additional crystals (0.5 g.) of VI (m. p. 121~122°C) were recovered. Further storage of the mother liquor of the second crop at room temperature for 3 months afforded the third crop which was recrystallized from ethanol to yield short prisms of VI (1.9 g.), m. p. 121~122°C. The total yield of VI was 12.6%. On admixing with a sample of I, the m. p. of VI was depressed.

Found: C, 45.77; H, 7.50; N, 6.42. Calcd. for $C_8H_{16}O_3NCl$: C, 45.82; H, 7.69; N, 6.68%.

Ethyl 5-Dimethylamino-3-ketopentane-1-carboxylate Hydrochloride (II).—A mixture of I (2.0 g.) and absolute ethanol (80 cc.) was saturated with dry hydrogen chloride and allowed to stand overnight. The ethanol was removed by distillation at about 40°C under reduced pressure and the residue was dried in a desiccator over phosphorous pentoxide. The resulting crystals were dissolved in a small quantity of ethanol by gentle warming and the solution was diluted with absolute ether, whereupon there separated a crystalline precipitate of ethyl 5-dimethylamino-3-ketopentane-1-carboxylate hydrochloride (II); yield 1.8 g. (80%). On recrystallization from absolute ethanol-absolute ether, colorless plates of m. p. 105~107°C were obtained and found to be hygroscopic.

Found: N, 6.02. Calcd. for $C_{10}H_{20}O_3NCl$: N, 5.89%.

Ethyl δ-Methylenelevulinate (III)*.—A sample of 1.5 g. of II was placed in a round-bottom flask and heated at 150°C in an oil bath under highly reduced pressure (0.002 mmHg). Colorless liquid with the characteristic smell of III was obtained in a receiver cooled in a dry ice-methanol bath; yield 0.6 g. (61%), λ_{max}^{MeOH} 210 (ε 10650) and 315 mμ (ε 27).

Found: C, 61.58; H, 7.14. Calcd. for $C_7H_{12}O_3$: C, 61.52; H, 7.75%.

Hydrogenation of III to Ethyl γ-Keto-*n*-caproate (V).—A sample (III) (440 mg.) in ethanol (3 cc.) absorbed hydrogen (75 cc. at 11°C, 753.7 mmHg) in the presence of platinum oxide (40 mg.). The reduced product was purified by fractional distillation in vacuo to give 370 mg. of ethyl γ-keto-*n*-caproate (V), b. p. (bath temp.) 122~126°C/18 mmHg This was identified by formation of semicarbazone and 2,4-dinitrophenylhydrazone by the usual procedure. Semicarbazone was recrystallized from ethyl acetate-petroleum ether; m. p. 105~106.5°C. The reported m. p. 106°C[4].

Found: N, 19.25. Calcd. for $C_9H_{17}O_3N_3$: N, 19.52%. 2,4-Dinitrophenylhydrazone was recrystallized twice from ethanol; long, orange-yellow needles, m. p. 69.5~71.0°C.

Found; N, 16.67. Calcd. for $C_{14}H_{18}O_6N_4$: N, 16.56%.

δ-Methylenelevulinic Acid (IV).—A mixture of

* Methyl ester of the same acid was reported by I. N. Nazarov and S. I. Zavyalov, *Izvest, Akad, Nauk S. S. S. R., Otdel. Khim. Nauk*, **1952**, 289; *Chem. Abstr.*, **47**, 5364 (1953) and by C. Grundmann and W. Ruske, *Chem. Ber.*, **86**, 939 (1953).

4) M. Maire, *Bull. Soc. chim. France*, [4] **3**, 285 (1908).

370 mg. of III and 7.5 cc. of 1.5 N sulfuric acid was stirred at 30°C for 3 hr. The reaction mixture was cooled with ice and adjusted to pH 8 with a saturated solution of sodium bicarbonate and washed with three 5 cc. portions of ethyl acetate. The water-layer was adjusted to pH 2.0 and extracted with three 6 cc. portions of ethyl acetate. After the extract has been dried over sodium sulfate, the ethyl acetate was removed by distillation under reduced pressure at 30°C to yield crude δ-methylenelevulinic acid, a colorless viscous liquid which is soluble in water; yield 50 mg. (17%). Ultraviolet spectrum of this compound in water showed the presence of a α,β-unsaturated ketone group at 212 mμ. However, purification of the product was unsuccessful. The analytically pure sample of IV has been obtained directly by thermal degradation of 5-dimethylamino-3-ketopentane-1-carboxylic acid hydrochloride (I) as described below.

A sample of 5 g. of I was heated (bath temp. 185°C/0.0075 mmHg) as described in the preparation of III to give a solid mass of crystals intermixed with oil in a receiver cooled in a dry ice-methanol bath. The crystals were drained on porous porcelain to remove the oily part; yield 1.26 g. (41.2%), m. p. 34.0~42.5°C*. The product was soluble in methanol, ether and water. Recrystallization from ether gave an analytical sample of δ-methylenelevulinic acid (IV), m. p. 44.0~45.5°C, $\lambda_{max}^{H_2O}$ 212 mμ (ε 9870) and 305 mμ (ε 30.3), ν_{max}^{Nujol} 1701 (conjugated carbonyl), 1644 (C=C), 2700~2500 (carboxyl OH) and 1724 cm^{-1} (carboxyl C=O).

Found: C, 55.97; H, 6.24. Calcd. for $C_6H_8O_3$: C, 56.24; H, 6.29%.

Semicarbazone. — m. p. 152~153°C (decomp.), λ_{max}^{MeOH} 262 mμ (ε 16200).

Found: C, 45.27; H, 5.98; N, 22.67. Calcd. for $C_7H_{11}O_3N_3$: C, 45.40; H, 5.99; N, 22.69%.

ε,ε'-Dithio-di-γ-keto-*n*-caproic Acid (IV').—δ-Methylenelevulinic acid (IV) (760 mg.) was added to a 4.12 M aqueous solution (1.45 cc.) of sodium tetrasulfide with stirring. The reaction was exothermic and the resulting orange-red solution was allowed to stand overnight at room temperature, and then adjusted to pH 7.4 with concentrated hydrochloric acid. After removal of the separated sulfur, the filtrate was shaken with three 10 cc. portions of ethyl acetate. The water-layer was adjusted to pH 4.0 and extracted with five 10 cc. portions of ethyl acetate. The dried extract was concentrated in vacuo to afford a crystalline mass (820 mg.). A mixture of the crude product and water was adjusted to pH 7.0 with sodium bicarbonate, filtered off the precipitated sulfur and then acidified to pH 4.0. The resulting precipitate was collected and washed with water, yield 429 mg. (45%). Recrystallization from ethyl acetate and then absolute ethanol resulted pure ε,ε'-dithio-di-γ-keto-*n*-caproic acid; yield 180 mg., m. p. 131~131.5°C.

Found: C, 44.50; H, 5.48. Calcd. for $C_{12}H_{18}O_6S_2$: C, 44.73; H, 5.60%.

Ozonolysis of IV. — (a) A solution of IV (200 mg.) in ethyl acetate (10 cc.) was treated with an approximately 3% by weight ozone-oxygen mixture at 0°C at a rate of 500 cc./min. for 30 min. To the resulting solution was added water (10 cc.) and zinc dust (300 mg.). The mixture was refluxed on a water bath for 30 min. The reaction mixture was filtered, while hot, into a solution of methone (300 mg.) in 10 cc. of ethanol. Dilution with water (20 cc.) afforded needless of (200 mg., 44%), m. p. 185~187°C. Recrystallization from aqueous methanol gave pure crystals of m. p. 188~189.5°C. The m. p. was undepressed on admixing with an authentic sample of formaldehyde methone. This established the presence of the terminal methylene group in IV. (b) A solution of IV (300 mg.) in ethyl acetate (15 cc.) was treated with 3% ozone-oxygen at −20°C at a rate of 400 cc./min. for 2 hr. The resulting yellow solution was concentrated to about 0.8 cc. in vacuo below 10°C, then 30% hydrogen peroxide (1.7 cc.) was added. After gentle warming of the mixture at 60°C for a little while, the resulting solution was kept at room temperature overnight. The colorless solution was evaporated under reduced pressure. Addition of water to the residue followed by evaporation was repeated to remove exess of hydrogen peroxide as much as possible. The final crystalline residue (320 mg.) gave only the distinct spot of succinic acid on paper chromatography[5] using xylene-phenol-85% formic acid (7:3:1) as a solvent. Recrystallization from ethanol gave 194 mg. (70%) of a pure sample of succinic acid, m. p. 183~184°C; mixed m. p. determination showed no depression.

β-Methylenelevulinic Acid (VII).—A sample of 4 g. of VI was heated (bath temp. 180°C/0.002 mmHg) as described in the preparation of III to give a crystalline product in a receiver cooled in a dry ice-methanol bath. A small amount of oily material was removed by treatment on a porous porcelain; yield 1.7 g. (69.5%), m. p. 62~66°C. Recrystallization from ether followed by fractional vacuum sublimation (60°C/0.06 mmHg) afforded an analytical pure sample; m. p. 67.0~68.5°C; $\lambda_{max}^{H_2O}$ 218~219 (ε 7520) and 309 mμ (ε 38.5); ν_{max}^{Nujol} 1682 (conjugated carbonyl), 1640 (C=C), 2800~2500 (carboxyl OH), and 1715 cm^{-1}, (carboxyl C=O).

Found: C, 56.29; H, 6.11. Calcd. for $C_6H_8O_3$: C, 56.24; H, 6.29%.

Ca Salt.—Found: C, 48.70; H, 4.72; Ca, 13.83. Calcd. for $C_{12}H_{14}O_6Ca$: C, 48.91; H, 4.80; Ca, 13.62%.

Semicarbazone.—M. p. 184°C (decomp.). Found: C, 45.38; H, 5.71; N, 22.44. Calcd. for $C_7H_{11}O_3N_3$: C, 45.40; H, 5.99; N, 22.69%.

2, 4-Dinitrophenylhydrazone. — M. p. 210°C (decomp.)[6]. Found: C, 46.66; H, 4.15; N, 18.25. Calcd. for $C_{12}H_{12}O_6N_4$: C, 46.76; H, 3.92; N, 18.18%.

Ozonolysis of VII was carried out in the same manner as described in the ozonolysis of IV: (a) The compound VII (99 mg.) gave formaldehyde methone (96 mg., 42.5%), indicating the presence

* B. p. of this compound was reported by H. T. Taylor, *J. Chem. Soc.*, **1958**, 3922.

5) N. F. Holyer and B. C. L. Weedon, *Chem. and Industry*, (1955), 1219. H. Kalbe, *Z. physiol. Chem.*, **297**, 19 (1954).

6) The same m. p. was reported by L. Birkofer and L. Storch, *Chem. Ber.*, **87**, 571 (1954).

of terminal methylene group. (b) The compound (346 mg.) gave a crude crystalline product (250 mg.) which gave only the distinct spot of malonic acid on paper chromatography. Pure malonic acid was obtained by fractional vacuum sublimation, m. p. and mixed m. p. 134~135°C (decomp.).

Separation of 6-Dimethylamino-4-ketohexane-1-carboxylic Acid Hydrochloride (VIII) and 3-(Dimethylaminomethyl)-4-ketopentane-1-carboxylic Acid Hydrochloride (XII) from Mannich Reaction Product.—A mixture of 5-ketocaproic acid[7] (30 g.) and dimethylamine hydrochloride (20.2 g.) was heated to 114°C in an oil bath. To the resulting melt was added paraformaldehyde (7 g.) and then the mixture was stirred at 114°C for 1.5 hr. After evaporation under reduced pressure, the resulting syrup was dissolved in absolute ethanol (35 cc.) by warming. To the cooled solution was added acetone (100 cc.) and some seeds of pure VIII, and the mixture was allowed to stand in a refrigerator for 3 days to give the first crystalline crop, which was separated and washed with a mixture of acetone-ethanol (14 : 5); yield 15.8 g., m. p. 98~108°C. Recrystallization from ethanol (18 cc.) gave a pure sample of VIII; yield 13.9 g. (27%), m. p. 116~117°C.

Found: C, 48.49; H, 7.90; N, 6.18. Calcd. for $C_9H_{15}O_3NCl$: C, 48.32; H, 8.11; N, 6.26%.

A sample of VIII (50 mg.) was added by bits to 1 cc. of fuming nitric acid. The reaction mixture was heated on a water bath until the evolution of nitrogen oxide ceased. After concentration, the reaction mixture was diluted with water and evaporated to dryness. The residue was dissolved in water. Aliquots of the solution were used for paper chromatography in the same manner as described above to give the spots of glutaric acid and succinic acid.

The mother liquor of the above mentioned first crop was stored in a refrigerator for 2 weeks to afford the second crop, which was collected and washed with acetone-ethanol and dried; yield 7.6 g. Recrystallization from ethanol gave a pure sample of XII; yield 6.6 g. (11.3%), m. p. 131~132°C. Iodoform test was positive.

Found: C, 48.53; H, 8.00; N, 6.44. Calcd. for $C_9H_{15}O_3NCl$: C, 48.32; H, 8.11; N, 6.26%.

4-Keto-5-hexene-1-carboxylic Acid (XI).—A sample of 5 g. of VIII was heated (bath temp. 185~190°C/0.005 mmHg) in the same manner as described in the preparation of III to give a crystalline product (2 g.) in a receiver in a dry ice-methanol bath. The product melted at room temperature into a colorless viscous liquid which was very hygroscopic and, on standing in atmosphere, formed a crystalline monohydrate. To the liquid product (2 g.) was added water (0.27 cc.) and the resulting crystalline monohydrate of XI was collected by filtration under ice-cooling, dried on a porous sheet; yield 1.4 g. (39%), m. p. 43~45°C. Cautious recrystallization from water gave a pure sample of monohydrate of XI; yield 1.2 g. (31%), m. p. 45.0~46.5°C. $\lambda_{max}^{H_2O}$ 212~3 (ε 8190) and 310~3 mμ (ε 29.6), ν_{max}^{Nujol} 1692 (conjugated carbonyl), 1617 (C=C), 2700~2500 (carboxyl OH), 1746 (carboxyl C=O) and 3600~3350 cm^{-1} (crystalline water).

(a) Crystalline monohydrate; Found: C, 52.46; H, 7.52. Calcd. for $C_7H_{10}O_3 \cdot H_2O$: C, 52.49; H, 7.55%. (b) Anhydrous acid (dried at 100°C/10 mmHg for 4 hr.); Found: C, 59.57; H, 7.35. Calcd. for $C_7H_{10}O_3$: C, 59.14; H, 7.09%. (c) Calcium salt* (dried at 125~130°C/10 mmHg for 4 hr.); Found: C, 51.71; 5.87; Ca, 12.42. Calcd. for $C_{14}H_{18}O_6Ca$: C, 52.16; H, 5.62; Ca, 12.43%.

Semicarbazone.—M. p. 156~157°C (decomp.), λ_{max}^{MeOH} 260 mμ (ε 17100).

Found: C, 47.62; H, 6.33; N, 21.18. Calcd. for $C_8H_{13}O_3N_3$: C, 48.23; H, 6.58; N, 21.09%.

Ozonolysis of XI was carried out in the same manner as described in the ozonolysis of IV: (a) The monohydrate (200 mg.) gave formaldehyde methone (148 mg., 40.5%). (b) The monohydrate (426 mg.) gave a crude crystalline product (245 mg., 70%) which gave only the distinct spot of glutaric acid on paper chromatography. Recrystallization from benzene gave pure glutaric acid; m. p. and mixed m. p. 95~96°C.

4-Keto-3-methylenepentane-1-carboxylic Acid (XIII).—A sample of 2 g. of XII was heated (bath temp. 175~180°C/0.002 mmHg) as described in the preparation of III to give a crystalline product; yield 0.9 g. (71%), m. p. 56~62°C. Three recrystallizations from ether gave a pure sample of XIII, m. p. 66~67°C, $\lambda_{max}^{H_2O}$ 222 (ε 8270) and 308 mμ (ε 39.5), ν_{max}^{Nujol} 1648 (conjugated carbonyl), 1631 (C=C), 2800~2500 (carboxyl OH) and 1738 cm^{-1} (carboxyl C=O).

Found: C, 59.22; H, 6.92. Calcd. for $C_7H_{10}O_3$: C, 59.14; H, 7.09%.

Semicarbazone.—M. p. 164~165°C (decomp.), long needles.

Found: C, 48.30; H, 6.38; N, 21.13. Calcd. for $C_8H_{13}O_3N_3$: C, 48.23; H, 6.58; N, 21.10%.

Ozonolysis of XIII was carried out in the same manner as described in the ozonolysis of IV: (a) The compound (100 mg.) gave formaldehyde methone (84 mg., 46%). (b) The compound (300 mg.) gave a crude crystalline product (295 mg.) which gave only the distinct spot of succinic acid on paper chromatography. Recrystallization from ethanol afforded 150 mg. (65%) of pure succinic acid, m. p. and mixed 183~184°C.

Methyl 6-Dimethylamino-4-ketohexane-1-carboxylate Hydrochloride (IX).—A mixture of VIII (3 g.) and absolute methanol (75 cc.) was saturated with dry hydrogen chloride and after-treatment was carried out just as described in the preparation of II. Recrystallization from absolute methanol-absolute ether gave long needles of IX (3 g., 95%), m. p. 91~93°C, very hygroscopic.

Found: N, 5.73. Calcd. for $C_{10}H_{20}O_3NCl$: N, 5.90%.

Methyl 4-Keto-5-hexene-1-carboxylate (X).—A sample of 2 g. of IX was heated (bath temp. 140~148°C/0.001 mmHg) in the same manner as described in the preparation of III. Yield 0.34 g. (26%), b. p.

7) H. Fittig and L. Wolff, *Ann.*, **216**, 129 (1883); W. H. Bentley and W. H. Perkin, *J. Chem. Soc.*, **69**, 1510 (1896).

* Prepared by Mr. T. Soga of Nikken Kagaku Co.

(bath temp.) 36~38°C/0.002 mmHg, λ_{max}^{MeOH} 209 mμ (ε 9570) and 320 mμ (ε 27.2), $\nu_{max}^{CCl_4}$ 1692 (conjugated carbonyl), 1617 (C=C) and 1746 cm^{-1} (ester C=O).

Found: C, 61.04; H, 7.56. Calcd. for $C_5H_{12}O_3$: C, 61.52; H, 7.75%.

Hydrolysis of X with dilute sulfuric acid in the same manner as described in the preparation of IV resulted a low yield of oily product, the ultraviolet absorption of which showed the presence of α,β-unsaturated ketone at 213 mμ in water. However, the product resisted an attempt to obtain a pure sample of 4-keto-5-hexene-1-carboxylic acid (XI).

Biological Activities.—δ-Methylenelevulinic acid (IV), β-methylenelevulinic acid (VII), 4-keto-5-hexene-1-carboxylic acid (XI) and 4-keto-3-methylenepentane-1-carboxylic acid (XIII) showed a potency of 0.6, 0.9, 0.4 and 1.3 units/mg. (in terms of sarkomycin potency) against *M. pyogenes var. aureus* 209-P, respectively. The ethyl ester III of IV and the methyl ester X of XI showed much higher potency than the original acids, but had higher toxicity than the original acid. LD_{50} of IV, VII, XI, XIII and III were 1.0, 3.7, 2.0, 4.7 and 0.78 mg./mouse, respectively. ε,ε'-dithio-di-γ-keto-*n*-caproic acid(IV') exhibited a curious activity; it inhibited strongly the growth of *Micrococcus flavus*, but had almost no activity against tested bacteria and fungi.

It is very interesting to find, that all these compounds possess antitumor activities against Ehrlich cells and HeLa cells[9]. The minimum necessary concentrations of IV, VII, XI and XIII for anti-HeLa cell effect were 62.5, 62.5, 12.5 and 62.5 mcg./cc. Against cells of Ehrlich carcinoma, IV, VII, XI and XIII had a potency of 1.56, 3.8, 2.2 and 3.4 units/mg. (in terms of sarkomycin potency) by cylinder plate method. The daily intraperitoneal injection of 0.5 mg./mouse/day of IV inhibited the ascites increase and prolonged the survival period of mice (highly inbred) bearing ascites type of Ehrlich carcinoma by intraperitoneal route. Especially, calcium salt of 4-keto-5-hexene-1-carboxylic acid (XI) showed an excellent results; daily intraperitoneal injection of 0.125, 0.25 or 0.5 mg./mouse/day which was continued for 52 days showed significant inhibition. The control mice all died in 14~22 days. Mice of the group treated with 0.5 mg. daily all survived 52 days. Moreover, toxicity of the calcium salt of XI was LD_{50}=4.0 mg./mouse.

A detailed report on the biological activities of the above-mentioned compounds will be published elswhere.

9) Private communicaiton from Professor H. Umezawa of National Institute of Health, Tokyo.

Summary

1) 2-(Dimethylaminomethyl)-3-ketobutane-1-carboxylic acid hydrochloride (VI) as well as 5-dimethylamino-3-ketopentane-1-carboxylic acid hydrochloride (I) has been obtained from levulinic acid, paraformaldehyde and dimethylamine hydrochloride by means of the Mannich reaction. Thermal degradation of I and VI afforded δ-methylenelevulinic acid (IV) and β-methylenelevulinic acid (VII), respectively.

2) 3-(Dimethylaminomethyl)-4-ketopentane-1-carboxylic acid hydrochloride (XII) as well as 6-dimethylamino-4-ketohexane-1-carboxylic acid hydrochloride (VIII) has been obtained from 5-ketocaproic acid, paraformaldehyde and dimethylamine hydrochloride by means of the Mannich reaction. Thermal degradation of XII and VIII afforded 4-keto-5-hexene-1-carboxylic acid (XI) and 4-keto-3-methylenepentane-1-carboxylic acid (XIII), respectively.

3) The structures of IV, VII, XI and XIII have been proven.

4) Some derivatives of above-mentioned carboxylic acids have been described.

5) It has been found that IV, VII, XI and XIII possess significant antitumor and antibacterial activites; especially calcium salt of 4-keto-5-hexene-1-carboxylic acid (XI) gave an excellent result in animal experiments.

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Department of Applied Chemistry
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*The Reaction of Tropoids and Quinone Derivatives. I. Reaction of Several Tropolones and p-Benzoquinone-dibenzenesulfonimide**

By Shuichi SETO, Hiromi YAMAZAKI and Yukio NISHIYAMA

(Received January 28, 1960)

Several processes have been reported for the synthesis of tropolones having an aryl group[1]. For example, as a method of introducing an aryl group into the 5-position of the tropolone ring, one by the decomposition of the diazonium salt obtained from 5-aminotropolone in benzene, anisole or allied compounds has been described, but the yield is generally not good.

Based on the work of Admas and others[2] that aryl phenylenediamide derivatives are obtained in good yields from quinonimide derivatives by their reactions with aromatic compounds, an attempt was made to apply this reaction to tropolones.

This reaction appears to be the action of quinonimide, acting as a kind of a cationoid reagent, on the aromatic compounds and it seems possible to apply this to tropoids other than tropolones.

Mixing of the chloroform solutions of tropolone and *p*-benzoquinonedibenzenesulfonimide (I) results in orange red solution. Addition of a small amount of triethylamine to this solution results in change of color of the solution to yellow and after some time, a colorless solid (II) separates.

This behavior is similar to the formation of 2-(4′-hydroxyphenyl)-*p*-phenylenedibenzenesulfonamide from phenol and I[3].

It is clear from its ultraviolet absorption spectrum, and coloration with ferric chloride that II possesses a tropolone ring, and its analytical values agree with those calculated for 2′,5′-dibenzenesulfonamidophenyltropolone.

From an analogy, to the reaction of phenol, the 2′, 5′-dibenzenesulfonamidophenyl-group is considered to have entered the *para*- or 5-position of the tropolone ring and the experimental results described below supports this assumption.

The same reaction carried out with 3-bromotropolone and 3, 7-dibromotropolone in place of tropolone respectively affords colorless crystals (III) and pale yellow crystals (IV), although the reaction velocity is somewhat slower than that in the case of tropolone itself. The analytical values of III and IV agree respectively with those for the monobromo and dibromo derivatives of II.

Hydrogenolysis of III and IV in the presence of palladium-charcoal affords II, and bromination of II and III in chloroform affords IV. These fact can be understood by assuming that the 2′, 5′-dibenzenesulfonamidophenyl group in II, III and IV is situated in the 5-position of the tropolone ring.

The reaction of I and 4-isopropyltropolone (hinokitiol) is likely to be affected by steric hindrance of the isopropyl group in the 4-position, but the reaction actually progressed smoothly, giving colorless crystals (V). Further, reaction of I with 3-bromo-6-isopropyltropolone and 3, 7-dibromo-4-isopropyltropolone respectively afforded colorless crystals (VI) and pale yellow crystals (VII).

Hydrogenolysis of VI and VII gave V.

From the foregoing experimental facts, and from analytical values and ultraviolet absorption spectra of V, VI and VII, it is clear, that V is 4-isopropyl-5-(2′, 5′-dibenzenesulfonamidophenyl)tropolone, and VI and VII are respectively its monobromo and dibromo derivatives. The fact, that the aryl group enters the 5-position without interference of such a bulky group in 4-position suggests, that this reaction might be applied to the syntheses of tricyclic tropolone derivatives.

3-Isopropyltropolone (*α*-thujaplicin) also reacts easily with I to form 3-isopropyl-5-(2′, 5′-dibenzenesulfonamidophenyl)tropolone (VIII).

The reaction of tropolone derivatives with a substituent in the 5-position with I was then carried out. Addition of triethylamine to the chloroform solution of 5-methyltropolone and I resulted in gradual blackening of the solution. This color change is different from that observed, when the reaction is progressing as anticipated.

Colorless crystals separated on standing this reaction mixture and this substance was found to be the reduction product of I, i. e. *p*-phenylenedibenzenesulfonamide.

A part of the starting 5-methyltropolone was recovered from the filtrate.

*) Presented at the 49th Tohoku Local Meeting of the Chemical Society of Japan, Yamagata, June, 1959.

1) Cf. T. Nozoe, Festschrift Arthur Stoll, Birkhäuser A. G., Basel (1957) p. 746.

2) R. Adams and W. Reifschneider, *Bull. Soc. chim. France*, **1958**, 23.

3) R. Adams and D. C. Blomstrom, *J. Am. Chem. Soc.*, **75**, 3405 (1953).

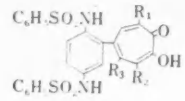

TABLE I. SOME PROPERTIES OF THE REACTION PRODUCTS

	R_1	R_2	R_3	M. p. °C (decomp.)	UV λ_{max}^{MeOH} mμ(log ε)
II	H	H	H	233~235	241(4.49), 345(4.15), 390(3.79)
III	Br	H	H	210~213	257(4.65), 351(4.29), 418(3.99)
IV	Br	Br	H	211~213	272(4.60), 356(4.31), 435(4.18)
V	H	H	isoPr	254~256	250(4.60), 344(4.24)
VI	Br	H	isoPr	242~243	263(4.58), 349(4.24), 413(3.93)
VII	Br	Br	isoPr	195~197	265(4.44), 355(4.06), 430(3.84)
VIII	isoPr	H	H	207~215	243(4.58), 340(4.28), 390(3.84)

The reaction of 5-bromotropolone and I also took the same course. It is known, that when the *para* position of phenol is blocked, as in *p*-cresol, the same reaction affords the reduction product, *p*-phenylenedibenzenesulfonamide[3,4].

I specifically attacks the *para* position of phenols and it is interesting, that it also attacks the 5-position of tropolones, corresponding to the *para* position, showing the similarity of phenols and tropolones.

Experimental[5]

5-(2',5'-Dibenzenesulfonamidophenyl)tropolone (II).—To a solution of 1 g. of *p*-benzoquinonedibenzenesulfonimide (I) dissolved in 25 ml. of chloroform, a solution of 0.8 g. of tropolone in 2 ml. of chloroform was added, by which the color of the solution changed to orange red. Addition of 3 drops of triethylamine to it further changed the color of the solution to yellow and colorless crystals began to separate after a few minutes. The mixture was allowed to stand for 1 hr. and the crystals were collected by filtration to 1.27 g. of the first crop of crystals, m. p. 228~232°C (decomp.). The filtrate was evaporated under a reduced pressure, 5 ml. of benzene and 2 ml. of 1 N sulfuric acid were added to the residue, and the crystals that separated out were collected by filtration. The crystals were washed with benzene and water, and amounted to 70 mg. of the second crop of m. p. 228~230°C (decomp.). The combined first and second crops of crystals were recrystallized from a mixture of chloroform and benzene to yield 1.30 g. of II of m. p. 233~235°C (decomp.).

Found: C, 59.20; H, 3.64; N, 5.30. Calcd. for $C_{25}H_{20}O_6N_2S_2$: C, 59.02; H, 3.97; N, 5.51%.

The filtrate left after separation of the second crop of crystals was combined with the washings, the benzene layer was separated, and evaporated under a reduced pressure. The residue was sublimed at 1 mmHg in a bath of 60°C, and 0.46 g. of tropolone was recovered.

4) R. Adams and K. R. Eilar, ibid., 73, 1149 (1951).

5) All melting points are uncorrected. The microanalyses were carried out by Mr. S. Ohyama and Miss Y. Endo of this Institute.

II was dissolved in ethyl acetate and aqueous solution of ferric chloride was added by which the organic layer colored red.

2-Acetoxy-5-(2',5'-dibenzenesulfonamidophenyl)-tropone.—A mixture of 100 mg. of II and 0.5 ml. of acetic anhydride was heated at 140°C for 20 min., by which II dissolved completely. The mixture was evaporated under a reduced pressure and the crystalline residue was recrystallized from chloroform to 60 mg. of crystals melting at 200~201°C.

Found: C, 58.85; H, 4.18; N, 5.03. Calcd. for $C_{27}H_{22}O_7N_2S_2$: C, 58.87; H, 4.03; N, 5.09%.

U. V. λ_{max}^{MeOH} mμ (log ε): 231(4.56), 330(4.11).

2-Methoxy-5-(2',5'-dibenzenesulfonamidophenyl)-tropone.—An ether solution of diazomethane was added to 100 mg. of II suspended in 4 ml. of methanol by which an active reaction set in with evolution of nitrogen. After standing the mixture over night, the crystals were collected and recrystallized from methanol, affording 70 mg. of colorless needles, m. p. 190~191°C.

Found: C, 60.36; H, 4.36; N, 5.27. Calcd. for $C_{26}H_{22}O_6N_2S_2$: C, 59.73; H, 4.24; N, 5.36%.

U. V. λ_{max}^{MeOH} mμ (log ε): 226(4.47), 330(4.11).

3-Bromo-5-(2',5'-dibenzenesulfonamidophenyl)-tropolone (III).—One drop of triethylamine was added to the solution of 130 mg. of 3-bromotropolone and 100 mg. of I dissolved in 5 ml. of chloroform and the mixture was allowed to stand for 2 days. The first crop of crystals that separated was collected by filtration to 50 mg. of crystals of m. p. 210~213°C (decomp.). The filtrate was evaporated under a reduced pressure, 2 ml. of benzene and 1 ml. of 1 N sulfuric acid were added and 90 mg. of the second crop of crystals, m. p. 205~212°C (decomp.), was obtained. The first and second crops of crystals were combined and recrystallized from chloroform-ethanol mixture to 135 mg. of crystals of m. p. 210~213°C (decomp.).

Found: C, 50.76; H, 3.26; N, 4.70. Calcd. for $C_{25}H_{19}O_6N_2BrS_2$: C, 51.08; H, 3.26; N, 4.77%.

The benzene layer was separated from the filtrate left after removal of the second crop of crystals, the solvent was evaporated, and the residue was sublimed at 1 mmHg in a bath of 100°C, by which 70 mg. of 3-bromotropolone was recovered.

3, 7-Dibromo-5-(2', 5'-dibenzenesulfonamidophenyl)tropolone (IV).—One drop of triethylamine was added to the solution of 180 mg. of 3, 7-dibromotropolone and 100 mg. of I dissolved in 5 ml. of chloroform and the mixture was allowed to stand for 5 days. The first crop of 160 mg. of crystals, m. p. 207~210°C (decomp.), was collected by filtration, the filtrate was evaporated, and 5 ml. of benzene and 1 ml. of 1 N sulfuric acid were added to its residue. The second crop of 10 mg. of crystals, m. p. 206~210°C (decomp.), thereby obtained was collected by filtration, combined with the first crop, and recrystallized from ethanol-chloroform mixture, affording 165 mg. of pale yellow crystals, m. p. 211~213°C (decomp.).

Found: C, 45.48; H, 2.71; N, 3.97. Calcd. for $C_{25}H_{19}O_6N_2Br_2S_2$: C, 45.03; H, 2.72; N, 4.20%.

The benzene layer was separated from the filtrate left after removal of the second crop of crystals, the solvent was evaporated, and the residue was sublimed at 1 mmHg and 120°C, from which 85 mg. of 3, 7-dibromotropolone was recovered.

Hydrogenolysis of III.—A solution of 90 mg. of III dissolved in 20 ml. of 0.1 N sodium hydroxide, added with 200 mg. of 5% palladium-charcoal, was shaken in hydrogen atomsphere at ordinary temperature. After the absorption of hydrogen ended, the catalyst was filtered off, the filtrate was acidified, and the precipitate thereby formed was crystallized from a mixture of ethanol and chloroform to 25 mg. of crystals, m. p. 230~233°C (decomp.), undepressed on admixture with II. The ultraviolet absorption spectra of these two substances were also in complete agreement.

Hydrogenolysis of IV.—A solution of 50 mg. of IV dissolved in 20 ml. of 0.1 N sodium hydroxide was added with palladium-charcoal. The mixture was treated as in the foregoing example. Recrystallization of the precipitate gave 15 mg. of crystals of m. p. 233~234°C (decomp.), undepressed on admixture with II. The ultraviolet absorption of this product was also in agreement with that of II.

Bromination of II.—A mixture of 60 mg. of bromine added to a suspension of 70 mg. of II in 5 ml. of chloroform was allowed to stand for 2 days and crystals were collected. This substance was found to be the unreacted II. The filtrate was evaporated under a reduced pressure and the oily residue solidified on being added with methanol. This solid was recrystallized from a chloroform-ethanol mixture to 10 mg. of pale yellow crystals, m. p. 207~210°C (decomp.), undepressed on admixture with IV. The ultraviolet absorption spectra of these two substances were also in good agreement. Admixture of this product with III melted at 195~200°C.

Bromination of III.—A suspension of 50 mg. of III in 5 ml. of chloroform, added by 60 mg. of bromine, was allowed to stand for 2 days. The reaction mixture was filtered to collect 30 mg. of crystals which was proved to be the unreacted III. The filtrate was treated as in the foregoing example and 10 mg. of pale yellow crystals, m. p. 207~209°C (decomp.), was obtained. This showed no depression of m. p. on admixture with IV.

4-Isopropyl-5-(2',5'-dibenzenesulfonamidophenyl)-tropolone (V).—One drop of triethylamine was added to the reddish orange solution formed by dissolving 110 mg. of 4-isopropyltropolone and 100 mg. of I in 4 ml. of chloroform and the color of the solution changed immediately to yellow, gradually separating colorless crystals. After allowing the mixture to stand for 30 minutes, the crystals were collected by filtration, affording 130 mg. of colorless crystals, m. p. 253~256°C (decomp.). The filtrate was evaporated under a reduced pressure, 5 ml. of benzene and 1 ml. of 1 N sulfuric acid were added to the residue, and 10 mg. of the second crop of crystals, m. p. 247~251°C (decomp.), was collected. The first and second crops of crystals were combined and recrystallized from a chloroform-ethanol mixture to 135 mg. of crystals, m. p. 254~256°C (decomp.).

Found: C, 60.36; H, 4.67; N, 4.90. Calcd. for $C_{25}H_{26}O_6N_2S_2$: C, 61.06; H, 4.76; N, 5.09%.

The benzene layer was separated from the filtrate left after removal of the second crop of crystals, the solvent was evaporated from it, and the residue was sublimed under a reduced pressure, from which 60 mg. of 4-isopropyltropolone was recovered.

3-Bromo-6-isopropyl-5-(2',5'-dibenzenesulfonamidophenyl)tropolone (VI).—An orange solution formed on dissolving 170 mg. of 3-bromo-6-isopropyltropolone and 100 mg. of I in 4 ml. of chloroform was added with one drop of triethylamine and the solution turned yellow but there was no precipitation of crystals. After allowing this mixture to stand for 7 days, the solvent was evaporated under a reduced pressure, leaving a mixture of crystals and oil. To this residue, 5 ml. of benzene and 1 ml. of 1 N sulfuric acid were added and crystals that separated out were collected to 150 mg. of colorless crystals, m. p. 242~243°C (decomp.).

Found: C, 53.21; H, 3.67; N, 4.10. Calcd. for $C_{25}H_{25}O_6N_2BrS_2$: C, 53.39; H, 4.00; N, 4.45%.

The benzene layer was separated from the filtrate left after removal of crystals, the solvent was evaporated from this layer, and sublimation of the residue under a reduced pressure gave 85 mg. of the recovered 3-bromo-6-isopropyltropolone.

3, 7-Dibromo-4-isopropyl-5-(2',5'-dibenzenesulfonamidophenyl)tropolone (VII).—To the yellow solution formed on dissolving of 400 mg. of 3, 7-dibromo-4-isopropyltropolone and 200 mg. of I in 8 ml. of chloroform, one drop of triethylamine was added and the solution changed transitrally red but returned immediately to the original yellow color. There was no precipitation of crystals after standing the mixture for 10 days. The solvent was evaporated under a reduced pressure from this mixture, 6 ml. of benzene and 1 ml. of 1 N sulfuric acid were added to the residue, and the crystallized residue was recrystallized from a chloroform-ethanol mixture to 330 mg. of pale yellow crystals, m. p. 195~197°C (decomp.).

Found: C, 47.62; H, 3.26; N, 3.73. Calcd. for $C_{25}H_{24}O_6N_2Br_2S_2$: C, 47.44; H, 3.42; N, 3.96%.

Evaporation of the benzene layer separated from the filtrate and low-pressure sublimation of its residue afforded 210 mg. of recovered 3, 7-dibromo-4-isopropyltropolone.

Hydrogenolysis of VI.—Hydrogenolysis of 50 mg. of VI in the same manner as for III afforded 30

mg. of crystals, m. p. 251~253°C (decomp.), undepressed on admixture with V.

Hydrogenolysis of VII.—Treatment of 100 mg. of VII as in the foregoing examples afforded 50 mg. of crystals of m. p. 251~253°C (decomp.), undepressed on admixture with V.

3-Isopropyl-5-(2',5'-dibenzenesulfonamidophenyl)-tropolone (VIII).—Treatment of 110 mg. of 3-isopropyltropolone and 100 mg. of I in the same manner as for V afforded 140 mg. of crystals of m. p. 207~215°C (decomp.).

Found: C, 61.92; H, 4.59; N, 4.84. Calcd. for $C_{25}H_{20}O_6N_2S_2$: C, 61.05; H, 4.76; N, 5.09%.

There was recovered 60 mg. of 3-isopropyltropolone.

Reaction of 5-Methyltropolone and I.—One drop of triethylamine was added to the solution of 40 mg. of 5-methyltropolone and 50 mg. of I dissolved in 2 ml. of chloroform by which the solution turned dark brown and crystals began to form after some time. The mixture was allowed to stand for 2 hr. and 20 mg. of colorless crystals, m. p. 240~241°C, were obtained. This showed no depression of m. p. on admixture with *p*-phenylenedibenzenesulfonamide and the ultraviolet absorption spectra of the two substances were identical.

Evaporation of the filtrate left an oily substance to which benzene and 1 N sulfuric acid were added, and the benzene layer was separated. The benzene solution was chromatographed over silica gel and 20 mg. of 5-methyltropolone was recovered from it.

Reaction of 5-Bromotropolone and I.—One drop of triethylamine was added to the solution of 30 mg. of 5-bromotropolone and 20 mg. of I dissolved in 2 ml. of chloroform by which the color of the solution changed through dark green to dark brown. The reaction mixture was treated as above, and 15 mg. of *p*-phenylenedibenzenesulfonamide and 15 mg. of 5-bromotropolone were obtained.

Summary

The reaction of tropolones with *p*-benzoquinonedibenzenesulfonimide was carried out and the following points were observed.

1) The 2',5'-dibenzenesulfonamidophenyl group enters the 5-position of the tropolone ring, similar to the case of phenol.

2) The reaction proceeds in the same way in the case of 4-isopropyltropolone, without interference of the isopropyl group.

3) In the case of tropolones with a substituent in 5-position, reduction of *p*-benzoquinonedibenzenesulfonimide takes place.

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The Mannich Base of Troponoid and its Application. IV. The Synthesis of Tropolon-5-ylalanine

By Shuichi SETO and Kyozo OGURA

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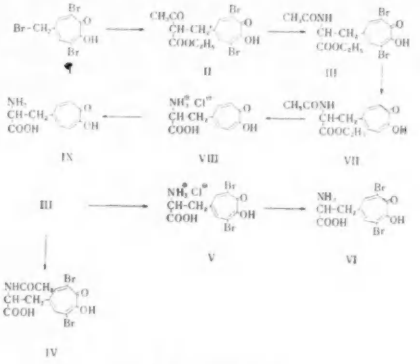
It was shown in previous reports[1,2] that 5-hydroxymethyl-, 5-formyl- and 5-bromomethyl-tropolone derivatives were derived from 3,7-dibromo-5-morpholinomethyltropolone and that 3,7-dibromo-5-formyltropolone and 3,7-dibromo-5-bromomethyltropolone (I) were important starting materials for the synthesis of various tropolone derivatives possessing a substituent in the 5-position of the tropolone ring. The present paper describes the synthesis of tropolone derivative possessing an amino acid residue in the 5-position of tropolone ring, i. e. tropolon-5-ylalanine, and related compounds from I.

Application of a large excess of ethyl potassioacetoacetate to I affords 3,7-dibromo-5-(β-acetyl-β-ethoxycarbonylethyl)tropolone (II)[2] whose Schmidt reaction gives 3,7-dibromo-5-(β-acetamido-β-ethoxycarbonylethyl)tropolone (III), m. p. 198°C. Hydrolysis of III with dilute alkali produces 3,7-dibromo-5-(β-acetamido-β-carboxyethyl)tropolone (IV), m. p. 217°C (decomp.), but the treatment of III with concentrated hydrochloric acid with boiling gives 3,7-dibromotropolon-5-ylalanine hydrochloride (V), m. p. 223~230°C (decomp.). Neutralization of V liberates 3,7-dibromotropolon-5-ylalanine (VI), m. p. 216°C (decomp.). Hydrogenolysis of III over palladium-carbon as a catalyst, in methanol affords 5-(β-acetamido-β-ethoxycarbonylethyl)tropolone (VII), m. p. 176°C. Treatment of VII with concentrated hydrochloric acid by boiling produces

1) S. Seto and K. Ogura, This Bulletin, 32, 493 (1959).
2) S. Seto and K. Ogura, ibid., 32, 1118 (1959).

tropolon-5-ylalanine hydrochloride (VIII), m. p. 215～220°C (decomp.), which liberates tropolon-5-ylalanine (IX), m. p. 240°C (decomp.), by neutralization. The amino acids so obtained, VI and IX, color reddish violet to ninhydrin and the aqueous layer turns green with ferric chloride. The infrared spectra of these compounds show absorption bands[3] originating in the zwitter ion structure characteristic of amino acid[1], by the presence of marked absorption at 3030, 1631 and 1575 cm^{-1} in VI and at 3020 and 1640 cm^{-1} in IX.



Experimental[5]

3, 7-Dibromo-5-(β-acetamido-β-ethoxycarbonylethyl)tropolone (III).— To a solution of 500 mg. of II dissolved in 25 ml. of benzene, 10 ml. of conc. sulfuric acid was added and the mixture was stirred under ice-cooling. To this mixture, 180 mg. of sodium azide was added and the stirring was continued for a further 1 hr. period, during which vigorous evolution of nitrogen gas occurred and the reaction product transited to the conc. sulfuric acid layer. The benzene layer was discarded, ca. 20 g. of cracked ice was added to the sulfuric acid layer, and the colorless precipitate thereby formed was collected by filtration. After washing the precipitate with water and drying, it was recrystallized from methanol and III was obtained as colorless needles, m. p. 197～198°C. Yield, 500 mg. The aqueous layer colored green to ferric chloride.

Found: C, 38.46; H, 3.62; N, 3.41. Calcd. for $C_{14}H_{15}O_5NBr_2$: C, 38.44; H, 3.43; N, 3.20%.

U. V. λ_{max}^{MeOH} mμ (log ε): 268 (4.50), 345 (3.99), 430 (3.88).

3, 7-Dibromo-5-(β-acetamido-β-carboxyethyl)tropolone (IV).—A solution of 50 mg. of III dissolved in 0.5 ml. of 10% sodium hydroxide solution was heated on a water bath for about 10 min. and cooled to room temperature when yellow crystals of the sodium salt separated out. The salt was neutralized with 6 N hydrochloric acid, the colorless crystals that formed were collected, and recrystallized from ethanol. Yield, 20 mg. of m. p. 216～217°C (decomp.).

Found: C, 35.10; H, 2.61; N, 3.44. Calcd. for $C_{12}H_{11}O_5NBr_2$: C, 35.21; H, 2.69; N, 3.42%.

U. V. λ_{max}^{MeOH} mμ (log ε): 268 (4.48), 345 (4.00), 425 (3.80).

3, 7-Dibromotropolon-5-ylalanine Hydrochloride (V).—A mixture of 150 mg. of III and 5 ml. of conc. hydrochloric acid was heated on a water bath for 2 hr. when the crystals dissolved completely. The solution was evaporated to dryness and residual colorless prismatic crystals were collected after addition of ethanol. Yield, 100 mg. of m. p. 223～230°C (decomp.).

Found: C, 30.11; H, 2.59; N, 3.38. Calcd. for $C_{10}H_{10}O_4NBr_2Cl$: C, 29.78; H, 2.48; N, 3.46%.

U. V. λ_{max}^{MeOH} mμ (log ε): 267 (4.47), 340 (3.88), 425 (3.66).

3, 7-Dibromotropolon-5-ylalanine (VI).—Adjustment of 50 mg. of V to pH 6 by addition of diluted ammonia water produced a pale yellow precipitate which was collected, washed with water, and recrystallized from ethanol to colorless crystals, m. p. 215～216°C (decomp.). Yield, 30 mg.

Found: C, 32.70; H, 2.45; N, 3.82. Calcd. for $C_{10}H_9O_4NBr_2$: C, 32.91; H, 2.76; N, 3.25%.

U. V. λ_{max}^{MeOH} mμ (log ε): 270 (4.85), 348 (4.09), 435 (4.90).

5-(β-Acetamido-β-ethoxycarbonylethyl)tropolone (VII).—A suspension of 1.5 g. of III in a solution of 0.6 g. of potassium hydroxide in 200 ml. of ethanol was shaken in hydrogen atmosphere after the addition of palladium-carbon catalyst. After absorption of 2 molar equivalents of hydrogen, the catalyst was filtered off and ethanol was evaporated completely from the filtrate. The residual, yellow potassium salt was dissolved in a small quantity of water and neutralized with 6 N hydrochloric acid, by which a yellow precipitate was produced. The mother liquor left after removal of the precipitate also afforded a small quantity of VII, m. p. 171～173°C, by extraction with ethyl acetate. Yield, 0.6 g.

Found: C, 59.42; H, 5.90; N, 5.01. Calcd. for $C_{14}H_{17}O_5N$: C, 60.20; H, 6.14; N, 5.02%.

U. V. λ_{max}^{MeOH} mμ (log ε): 231 (4.37), 228 (4.05).

Tropolon-5-ylalanine Hydrochloride (VIII).—A solution of 100 mg. of VII dissolved in 0.5 ml. of conc. hydrochloric acid was heated on a water bath for 1 hr. and the solution was evaporated to dryness, leaving a syrupy residue. The addition of ethanol to this residue resulted in crystallization, the crystals were collected, and recrystallized from ethanol. Yield, 50 mg. of m. p. 220°C (decomp.).

Found: C, 48.76; H, 5.27; N, 5.45. Calcd. for $C_{10}H_{12}O_4NCl$: C, 48.40; H, 4.84; N, 5.70%.

U. V. λ_{max}^{MeOH} (log ε): 229 (4.37), 326 (4.01).

Tropolon-5-ylalanine (IX).—A solution of 100 mg. of VIII dissolved in a small quantity of water was adjusted to pH 6 by addition of dilute ammonia water, the precipitate formed was collected, and recrystallized from ethanol. Yield, 40 mg. of m. p. 240°C (decomp.).

Found: C, 52.20; H, 5.77; N, 5.83. Calcd. for $C_{10}H_{11}O_4N \cdot H_2O$: C, 52.86; H, 5.77; N, 6.17%.

U. V. λ_{max}^{MeOH} mμ (log ε): 230 (4.31), 330 (4.00).

3) L. J. Bellamy, "The Infrared Spectra of Complex Molecules", Methuen, London (1958), p. 234.

4) K. Ogura and Y. Ikegami, *Bull. Chem. Research Inst. Non-Aqueous Solutions, Tohoku Univ.*, **9**, 23 (1959).

5) All melting points are uncorrected. The microanalyses were carried out by Mr. S. Oyama and Miss Y. Endo of this Institute.

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Infrared Spectra of Diacetyl Monoxime and Isonitrosoacetone

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Oximes are known to be subject to association, which has hampered the elucidation of the molecular structures of this type of compounds by means of physical methods such as dipole moment measurement, etc. The association through hydrogen bonding is an interesting problem in its own right and extensive studies have been made on these compounds by means of infrared spectroscopy[1] and Raman effect and also by the freezing point depression[2] of solutions, X-ray analysis[3-6] on crystals, etc. For this purpose, it is desirable and even necessary to carry out as complete assignments as possible of observed frequencies to various modes of vibrations of characteristic groups. Two oximes having conjugated double bonds were chosen in the present study anticipating the possible increase of the effect of hydrogen bonding due to conjugation.

Materials

Diacetyl Monoxime.—A commerical preparation was purified by recrystallization from an aqueous solution (m. p. 74.5°C).

Isonitrosoacetone.—A commercial sample was purified by extraction from an ether solution with petroleum ether (m. p. 64.5°C).

Experimental

The infrared spectra were recorded with a Hilger H-800 infrared spectrophotometer equipped with a rock-salt prism as well as with a fluorite prism. Both these compounds were studied in carbon tetrachloride and in carbon bisulfide, no appreciable dependence of frequencies upon the kind of solvents being observed. For isonitrosoacetone, which was sparingly soluble in carbon tetrachloride and carbon bisulfide, also chloroform solutions were employed. The results are shown in Tables I and II.

The spectra of solutions of various concentrations, solid samples, and some of the deuterated compounds, CH_3-CO-CR-NOD (R=CH_3 or H), were also studied whenever they were required for carrying out assignments.

Discussion

The spectra of diacetyl monoxime and isonitrosoacetone in the wave number range from 3200 to 3600 cm^{-1} are reproduced in Figs. 1 and 2. They show a very strong sharp band at about 3570 cm^{-1} and a broad band at about 3330 cm^{-1}. The intensity of the former decreases, whereas that of the latter increases with increasing concentration. The former disappears completely in the solid state. These bands are absent in the spectra of the corresponding deuterated compounds, which display a new strong sharp band at about 2620 cm^{-1} along with a broad band at about 2470 cm^{-1}. These facts indicate that the band of diacetyl monoxime at 3577 cm^{-1} and that of isonitrosoacetone at 3574 cm^{-1} can be unequivocally assigned to the OH stretching vibration of free OH groups, while the band of the former compound at about 3345 cm^{-1} and that of the latter at about 3325 cm^{-1} can be assigned to the OH stretching vibration of hydrogen-bonded OH groups. These wave numbers suggest that

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1) A. M. Buswell, W. H. Rodebush and M. F. Roy, *J. Am. Chem. Soc.*, **60**, 2444 (1938).
2) A. Reiser, Symposium on Hydrogen Bonding held in Ljubljana, 1957. See also D. Hadži and H. W. Thompson, "Hydrogen Bonding", Pergamon Press, London (1959), p. 443.
3) T. K. Bierlein and E. C. Lingafelter, *Acta Cryst.*, **4**, 450 (1951).
4) Y. Okaya, A. Shimada and I. Nitta, This Bulletin, **29**, 210 (1956).
5) D. E. Williams, G. Wohlauer and R. E. Rundle, *J. Am. Chem. Soc.*, **81**, 755 (1959).
6) L. E. Godycki and R. E. Rundle, *Acta Cryst.*, **6**, 487 (1953).

Table I. Infrared absorption of diacetyl monoxime

Wave number cm^{-1}	Intensity	Assignment
3577	strong	OH stretching (free)
3345	strong, very broad	OH stretching (assoc.)
3065	weak, broad	CH_3 degenerate stretching
2945	weak, broad	CH_3 symmetric stretching
1698	strong	CO stretching (free)
1686	shoulder	CO stretching (assoc.)
1630	weak	CN stretching
1424	medium, broad	CH_3 degenerate deformation
1365	strong	CH_3 symmetric deformation
1355	strong	OH in-plane bending (free)
1304	weak	CC(central) stretching (assoc.)
1298	weak	CC(central) stretching (free)
1124	strong	CH_3 in-plane rocking
1022	strong	CH_3 in-plane rocking
970	weak	NO stretching (assoc.)
963	weak	NO stretching (free)
933	weak	C-CH_3 stretching

Table II. Infrared absorptions of isonitrosoacetone

Wave number cm^{-1}	Intensity	Assignment
3574	strong	OH stretching (free)
3325	strong, broad	OH stretching (assoc.)
1703	strong	CO stretching (free)
1674	strong	CO stretching (assoc.)
1614	medium	CN stretching
1450	medium	CH_3 degenerate deformation
1398	strong	OH bending (free)
1366	strong	CH_3 symmetric deformation
1320	very weak	CC(central) stretching
1226	strong	CH in-plane bending
1016	strong	CH_3 in-plane rocking
990	strong	NO stretching (assoc.)
972	strong	NO stretching (free)
920	medium	C-CH_3 stretching
835	weak	CH out-of-plane bending

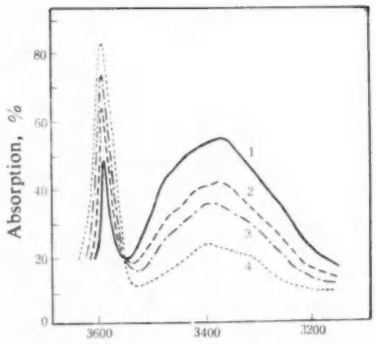

Fig. 1. Diacetyl monoxime in carbon tetrachloride.
1) 0.312 mol./l., 0.010 cm. cell. 2) 0.078 mol./l., 0.040 cm. cell. 3) 0.039 mol./l., 0.080 cm. cell. 4) 0.010 mol./l., 0.320 cm. cell.

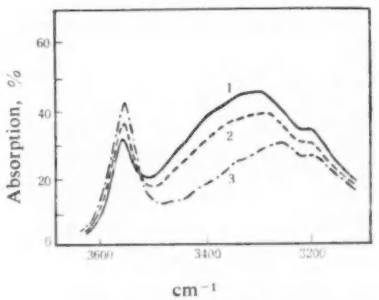

Fig. 2. Isonitrosoacetone in chloroform.
1) 0.901 mol./l., 0.002 cm. cell. 2) 0.340 mol./l., 0.004 cm. cell. 3) 0.021 mol./l., 0.064 cm. cell.

intermolecular hydrogen bondings are involved in association, because the stretching vibration of OH groups forming a chelate ring is known[7] to absorb at a frequency much lower than 3300 cm^{-1}.

The value of about 3570 cm^{-1} for the wave number of stretching vibration of free OH groups is fairly low compared with those of alcohols ranging in 3600~3650 cm^{-1} and is rather close to those of carboxylic acids at about 3600 cm^{-1}. Oximes having no conjugate double bonds, such as acetaldoxime, acetoxime, cyclohexanoxime, etc.[8] absorb at about 3600 cm^{-1} in solutions, while those containing conjugate double bonds show absorptions at lower frequencies. For instance, benzaldoxime and its derivatives absorb in the wave number range 3500~3560 cm^{-1} in solutions,* and quinone monoxime[10] at 3540 cm^{-1}. The present results are consistent with this relation. On the other hand, the values of 3345 cm^{-1} and 3325 cm^{-1} for the wave numbers of stretching vibrations of hydrogen-bonded OH groups of the two compounds under investigation are higher than those of the oximes mentioned above, most of which absorb at a wave number lower than 3300 cm^{-1}**.

Three types of hydrogen bonds can be presumed, namely –OH···N–C, –OH···O–N= and –OH···O–C–. The type of association will be discussed below in connection with other absorption bands. As can be anticipated, Raman spectra show no line corresponding to OH stretching vibration or only a very weak line[11,12].

The weak broad bands at 3065 and 2945 cm^{-1} of diacetyl monoxime were assigned to the degenerate and symmetric stretching vibrations of methyl groups, respectively. The appearance of these bands observed in solutions were not altered appreciably on solidification or on deuteration. The corresponding bands and the CH stretching vibration of isonitrosoacetone were too weak to be observed with certainty. Therefore, they are not listed in Table II.

The spectra in the wave number range covering 1600~1700 cm^{-1} are shown in Figs. 3 and 4. Diacetyl monoxime has a very strong band at 1698 cm^{-1} with a shoulder at 1686 cm^{-1}. The corresponding band of isonitrosoacetone split into two peaks, a main peak being found at 1703 cm^{-1} and a subsidiary one at 1674 cm^{-1}. Besides, a relatively weak band appeared at 1630 cm^{-1} in the spectrum of diacetyl monoxime and at 1614 cm^{-1} in that of isonitrosoacetone. The general features of these bands were not affected by deuteration, except for slight changes taking place in the

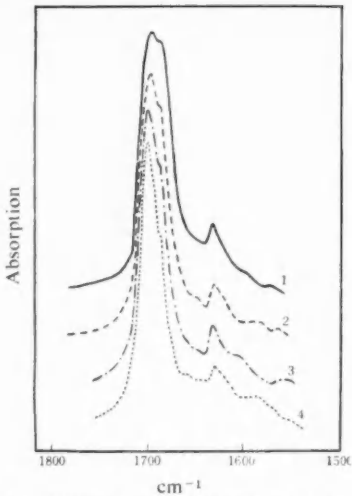

Fig. 3. Diacetyl monoxime in carbon tetrachloride.
1) 0.312 mol./l., 0.010 cm. cell. 2) 0.078 mol./l., 0.040 cm. cell. 3) 0.039 mol./l., 0.080 cm. cell. 4) 0.020 mol./l., 0.160 cm. cell. In this and subsequent figures, the ordinates of curves are shifted from one another for the sake of clarity.

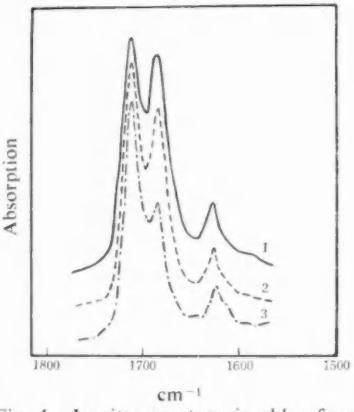

Fig. 4. Isonitrosoacetone in chloroform.
1) 0.901 mol./l., 0.002 cm. cell. 2) 0.340 mol./l., 0.004 cm. cell. 3) 0.021 mol./l., 0.064 cm. cell.

7) L. J. Bellamay, "The Infrared Spectra of Complex Molecules", 2nd Ed., Methuen, London (1958).
8) S. Califano and W. Lüttke, *Z. physik. Chem.* (neue Folge), **5**, 240 (1956).
9) A. Palm and H. Werbin, *Can. J. Chem.*, **31**, 1004 (1953).
10) D. Hadži, *J. Chem. Soc.*, **1956**, 2725.
* The values of wave numbers observed by Palm and Werbin[9] are distributed over a wide range, no characteristic tendency being found for the present.
** Califano and Lüttke[8] reported a value of 3315 cm^{-1} for *syn*-benzaldoxime, while Palm and Werbin[9] observed a band at 3270 cm^{-1} for *β(anti)*-benzaldoxime in a chloroform solution.
11) M. Milone, *Gazz. chim. ital.*, **67**, 527 (1937).
12) L. Kahovec and K. W. F. Kohlrausch, *Ber.*, **75**, 1541 (1942).

position of absorption bands. In general, saturated open chain ketones absorb in the range of 1705~1725 cm^{-1}, while compounds having a C=N bond show an absorption in the range of 1640~1690 cm^{-1}, provied that the compounds have an open chain or that they have a ring system involving no conjugation. Although the frequencies of CO and CN stretching vibrations may shift to some extent in conjugate systems, it is still reasonable to presume that the CO stretching vibration has a higher frequency than that of the CN stretching vibration. In addition, a band due to the CO stretching vibration is, in general, very strong, whereas a band due to the CN stretching is not always so. For these reasons, the bands at about 1700 cm^{-1} were assigned to the CO stretching vibration and those at about 1620 cm^{-1} to the CN stretching mode.

Kahovec and Kohlrausch[12] observed two Raman frequencies, 1679 and 1632 cm^{-1}, of diacetyl monoxime in the crystalline state. They tentatively assigned these frequencies to the CO stretching and the CN stretching vibration, respectively, with due precaution to the low value of the latter frequency compared with those of acetaldoxime, etc.[11,13,14] at about 1670 cm^{-1}. Their assignments seem to be adequate, because strong conjugation in a molecule will lower the characteristic frequency associated with a double bond. In fact, Hadži[10] observed the CO band of 1, 4-benzoquinone monoxime at 1628 cm^{-1} in the solid state and at 1648 cm^{-1} in solutions and also the CN band at 1555 cm^{-1} in the solid state. Palm and Werbin[9] have made observations on the CN frequencies of benzaldoxime and its derivatives in the solid state, the observed values ranging from 1614 to 1650 cm^{-1}.

The CO bands mentioned above showed a decrease in intensity of the main peak and an increase in that of the subsidiary peak or the shoulder with increasing concentration. The effect of association on the CO stretching frequency is presumed to cause a shift towards a lower frequency owing to the increased single bond character of the C=O bond due to hydrogen bond formation. Accordingly, the main peaks were assigned to the stretching vibration of free CO groups while the subsidiary peak and the shoulder were assigned to that of hydrogen-bonded CO groups. This suggests that hydrogen bonds of the -OH···O=C- type are present in solutions.

The absorption spectrum of diacetyl monoxime in the wave number range 1300~1500 cm^{-1} is shown in Fig. 5. A band at about

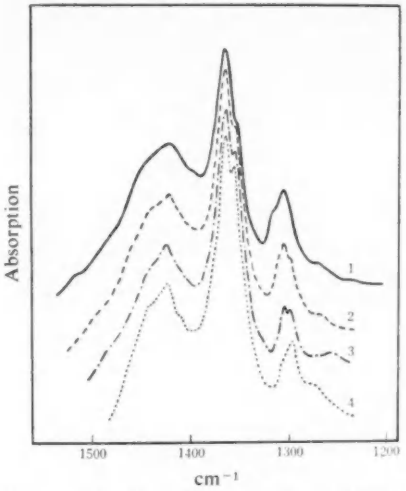

Fig. 5. Diacetyl monoxime in carbon tetrachloride.

The concentrations and the cell lengths are the same as given in Fig. 3.

1424 cm^{-1} is a broad one of medium intensity. A strong band 1365 cm^{-1} had a shoulder, which changed into a distinct maximum at 1355 cm^{-1} with increasing dilution. The same compound in the solid state showed a broad band at about 1430 cm^{-1} and a sharp one at 1365 cm^{-1}, no peak or shoulder being observed at about 1355 cm^{-1}. The change of spectral features taking place on deuteration was inappreciable, except that the band at 1355 cm^{-1} disappeared and a new band appeared at about 1000 cm^{-1}, although it overlapped with other bands. Based on these experimental facts, the band at 1355 cm^{-1} was assigned to the bending vibration of free OH groups. Palm and Werbin[15] proposed to assign a band of $\alpha(syn)$-benzaldoxime at 1265 cm^{-1} to the OH in-plane bending vibration, Hadži[10] assigned a band of quinone oxime near 1450 cm^{-1} to the OH bending vibration, and Bratož et al.[16] found the values of 1460 and 1078 cm^{-1} for the OH and OD bending vibrations, respectively. These results suggest the adequacy of the present assignments.

Two bands at 1424 and 1365 cm^{-1} mentioned above were assigned to the CH_3 degenerate and symmetric deformation vibrations, respectively, because they showed no concentration change and also because they were not affected by deuteration. The slight decrease of these frequencies below those of hydrocarbons is presumed to be a result of the presence of a C=O or C=N group in the molecule. In fact,

13) J. Goubeau, ibid., **68**, 912 (1935).
14) H. J. Bernstein and W. H. Martin, *Trans. Roy. Soc. Canada*, Sect. III, **31**, 105 (1937).
15) A. Palm and H. Werbin, *Can. J. Chem.*, **32**, 858 (1954).
16) S. Bratož, D. Hadži and G. Rossmy, *Trans. Faraday Soc.*, **52**, 464 (1956).

acetone[17] shows absorptions at 1430 and 1363 cm^{-1} and diacetyl at 1426 and 1362 cm^{-1} in the vapor state and at 1420 and 1352 cm^{-1} in the liquid state[18,19]. The Raman frequencies of diacetyl monoxime observed by Kahovec and Kohlrausch[12] correspond to these vibrational modes. The OH bending frequency of hydrogen-bonded OH groups was not observed clearly but, as suggested also by Califano and Lüttke[20] in their studies on formaldoxime and acetoxime, is expected to be masked by the band at 1424 cm^{-1}. In fact, this band became relatively weak and sharp with decreasing concentration as well as on deuteration.

Another band at about 1300 cm^{-1} appeared to consist of two component peaks at 1304 and 1298 cm^{-1}. The former was stronger than the latter in concentrated solutions, whereas the intensity relation was reversed in dilute solutions. Accordingly, by taking into account the weak intensity of the band and the value of the wave number, the former was assigned to the C–C(central) stretching vibration of associated molecules, while the latter was assigned to that of unassociated ones. The increase of frequency displayed by associated molecules over that of unassociated ones can be readily explained, since the C–C bond in an associated molecule has a greater double bond character than the bond has in an unassociated molecule. This rather weak band due to the C–C stretching vibration has its counterpart in the Raman spectra observed by Kahovec and Kohlrausch[12], who observed a very strong Raman band at 1310 cm^{-1} in a chloroform solution and at 1315 cm^{-1} in the crystalline state. The value of 1300 cm^{-1} is fairly large for a C–C stretching vibration, but is nearly equal to 1284 cm^{-1} observed in the Raman spectra of diacetyl involving also the conjugation of double bonds[18,19].

In this wave number range, isonitrosoacetone absorbed in much the same way as diacetyl monoxime did. The spectra of the former differed from that of the latter only in that the absorption frequency due to the OH bending vibration at 1398 cm^{-1} and that due to the CH_3 degenerate deformation vibration overlapped each other. Accordingly, the latter was evaluated from the spectra of the solid or of the deuterated sample. The same precaution was also taken for the C–C stretching vibration, because it was very weak.

The vibrational modes expected to appear in the wave number range 800～1250 cm^{-1} are CH_3 in-plane and out-of-plane rocking vibrations, an NO stretching vibration, a C–CH_3 stretching vibration and an OH out-of-plane bending vibration. Isonitrosoacetone will show additional bands due to the CH in-plane and out-of-plane bending motions. Only a band arising from the NO stretching vibrations is possibly subject to an intensity change with concentration. A band having such a character was observed at 963～970 cm^{-1} for diacetyl monoxime (See Fig. 6.) and at 972～990 cm^{-1} for isonitrosoacetone.

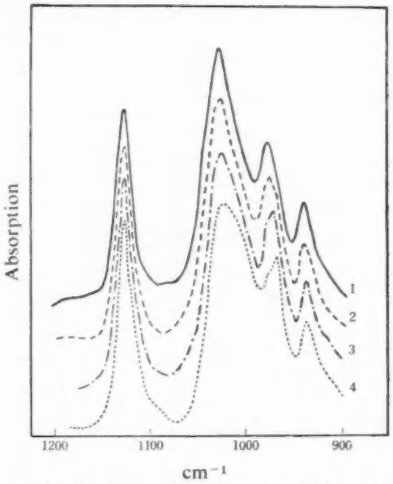

Fig. 6. Diacetyl monoxime in carbon tetrachloride.
1) 0.397 mol./l., 0.008 cm. cell. 2) 0.198 mol./l., 0.016 cm. cell. 3) 0.099 mol./l., 0.032 cm. cell. 4) 0.060 mol./l., 0.053 cm. cell.

The double bond character of the N–O bond will be greater in associated molecules than in unassociated ones. Accordingly, the increase in the amount of associated molecules with increasing concentration will give rise to an increase in the intensity of the component peak of higher frequency. This explains adequately the results of observations that with increasing dilution the maximum of these composite bands shifted towards the longer wavelength side. Hadži[10] assigned a band of 1, 4-benzoquinone monoxime at 1025 cm^{-1} while Palm and Werbin[15] assigned the bands of various oximes at about 940 cm^{-1} to the NO stretching vibration. The present assignment is in agreement with theirs.

A weak band of diacetyl monoxime at 933 cm^{-1} and that of isonitrosoacetone at 920 cm^{-1} were assigned to the C–CH_3 stretching vibration, reference being directed to a similar band of diacetyl at 945 cm^{-1}.

17) D. Price, *J. Chem. Phys.*, **9**, 725 (1941).
18) T. Miyazawa, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **74**, 743 (1953).
19) J. W. Sidman and D. S. McClure, *J. Am. Chem. Soc.*, **77**, 6471 (1955).
20) S. Califano and W. Lüttke, *Z. physik. Chem.* (neue Folge), **6**, 83 (1956).

Isonitrosoacetone showed an absorption at 833 cm^{-1}, which had no counterpart in the spectrum of diacetyl monoxime. For this reason and also because the frequencies of out-of-plane vibrations are known to be lower than those of in-plane vibrations, this band was assigned to the CH out-of-plane bending vibration.

Bands still left to be assigned are those of diacetyl monoxime at 1124 and 1022 cm^{-1} and of isonitrosoacetone at 1226 and 1016 cm^{-1}. Since CH in-plane bending vibrations usually absorb at higher frequencies than CH_3 in-plane rocking vibrations do, the band at 1226 cm^{-1} was assigned to the CH in-plane bending mode and others to the CH_3 rocking modes.

For both diacetyl monoxime and isonitrosoacetone, the band near 1020 cm^{-1}, which was sharp in the solid state, showed a hump on the lower frequency side especially in dilute solutions. This suggests the presence of another band capable of being assigned to the OH out-of-plane bending vibration of unassociated molecules.

In this way, all major observed bands have been interpreted in terms of the molecular form of an oxime type, CH_3-CO-CR=NOH (R=CH_3 or H). If the molecules exist in a nitroso form, CH_3-CO-CHR-NO, bands ascribed to hydroxyl groups in the present investigation could hardly be explained adequately. In addition, the presence of a C-N bond and an N=O bond in a molecule of the nitroso form in place of a C=N bond and an N-O bond as in that of the oxime form will render proper assignments almost impossible. The coexistence of the two forms is also ruled out, because the spectra are simpler than might be expected for the presence of the two forms. This conclusion affords at least an element of simplification in dealing with these molecules by means of other physical methods of attack.

Summary

The infrared absorption spectra of diacetyl monoxime and isonitrosoacetone in solutions were recorded in the rock-salt region. The assignment of observed bands was carried out, taking into account the concentration dependence of the spectra, the effect of deuteration, and the absorptions in the solid state. All the observed frequencies could be interpreted in terms of the molecular form of an oxime type, the presence of molecules in a nitroso form being presumed to be unlikely.

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Spectroscopic Study on the Living Polymers of Styrene, Butadiene and their Derivatives

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Recently the living polymers of styrene[1-3,5-7], its derivatives, butadiene[4] and isoprene have been an object of investigation, in view of their interesting property as an initiator of polymerization of vinyl monomers.

Their structure which seems to be the origin of the red color and the reactivity has been the subject of considerable discussion[1,2,5]. For the living polymer of styrene Szwarc proposed a structure of polymer anion having two groups of benzyl anion type at both ends of the polymer chain[2]. However, no direct evidence has been shown for this structure.

In the present paper, comparing the spectra of the living polymers of styrene and its derivatives with that of alkali benzyl, the

1) G. Meshitsuka and Y. Okada, *Chemistry of High Polymers* (*Kobunshi-kagaku*), **14**, 33, 37, 123 (1957).
2) M. Szwarc, M. Levy and R. Milkovitch, *J. Am. Chem. Soc.*, **78**, 2655 (1956); M. Szwarc, *Nature*, **178**, 1168 (1956).
3) R. Wack, A. Rembaum, J. D. Coombes and M. Szwarc, *J. Am. Chem. Soc.*, **79**, 2026 (1957).
4) H. Brody, M. Ladacki, R. Milkovitch and M. Szwarc, *J. Polymer Sci.*, **25**, 221 (1957).
5) K. Hirota, K. Kuwata, H. Togawa and S. Ishida, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **79**, 602 (1958).
6) K. Hirota, K. Kuwata and K. Morigaki, This Bulletin, **31**, 538 (1958); **32**, 100 (1959).
7) K. Hirota and K. Kuwata, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **78**, 1421 (1957); K. Kuwata and K. Hirota, *Annual Reports of the Institute for Fibre Research* (*Sen-i Kagaku Kenkyu-jo Nen-po*), **11**, 20 (1958).

author is to report that their structure is a polymer anion with the end of benzyl anion type.

The existence of the living polymers of butadiene and isoprene was asserted by Szwarc et al.[4] In this paper, their structure and reactivity are to be discussed from the spectroscopic data on the living polymers prepared by the direct reaction of butadiene and isoprene with metallic sodium, and on the block polymerization of isoprene with the living polymers of styrene.

Experimental

Materials Used.—Since the living polymers have an extreme reactivity toward water, oxygen, and carbon dioxide, special precautions on purifications of the starting materials are required[5,7]. In addition to the ordinary method of purification the monomers (styrene, α-methyl styrene, *p*-methyl styrene and *p*-divinyl benzene) were dried over metallic sodium for several hours and then distilled into storage vessels under reduced pressure. The solvents, tetrahydrofuran (THF), dioxane and toluene, were refluxed over metallic sodium or potassium for several hours, and also distilled under reduced pressure into a glass ampoul containing a piece of sodium and a small amount of anthracene. The blue color appeared instantly and stayed permanently. The solvents were distilled under reduced pressure into the reaction vessel as required. For toluene, however, styrene was used instead of anthracene, since toluene is a poor solvent for sodium adduct of anthracene. Mercury dibenzyl, prepared by the Grignard reaction[8] between benzylmagnesium chloride with mercuric chloride, was purified by recrystallization from toluene. Diallyl ether of GR grade, dried over metallic sodium for a short time, was purified by distillation under reduced pressure.

Preparation of the Samples.—All the processes of preparations and measurements were carried out in the glass vessels which were previously degassed as much as possible. A typical method of preparation was as follows: Alkali metal was distilled under reduced pressure from an ampoul A into an ampoul B (see Fig. 1). Monomer or solvent was distilled into B from an ampoul C. Then the vessel was sealed off from the vacuum system. The reaction proceeded gradually and an intensely colored solution of the living polymer formed. This solution was filtered through a glass filter G and stored in an ampoul D. The solution of the living polymer or the anion formed was poured into the measuring cell E and was diluted by the solvent distilled from D until an appropriate concentration was obtained. The concentration of the living polymers of styrene and isoprene were determined by the flame spectroscopy of alkali metal contained in the solutions, and the molar extinction coefficients of the living polymers were estimated.

8) P. Wolff, *Ber.*, **46**, 64 (1913).

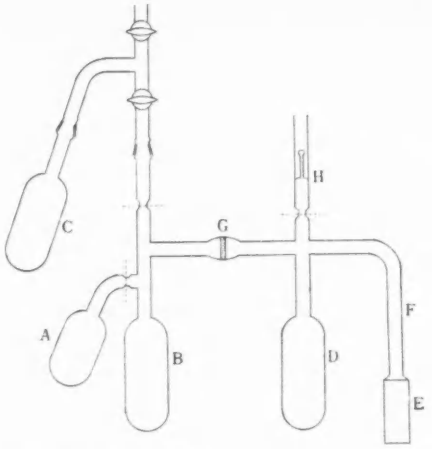


Fig. 1. Apparatus for preparation of the living polymers.
A, B, C and D: Glass ampoul, E: quartz cell, F: Gradual joint, G: Glass filter, H: Breakable joint.

Measurement of Absorption Spectra.—Absorption spectra of the living polymers and the anions were measured from 300 mμ to 2 μ with a Beckman DU type spectrophotometer equipped with an additional cover on the cell holder. After the measurement of the spectra, the vacuum was broken off and the spectra of the product were again measured.

Experimental Results

A spectrum between 300 mμ and 2 μ for the toluene solution of the living polymer of styrene is shown in Fig. 2. In addition to the characteristic absorption at 510 mμ which had already been reported[1,5] another absorption at 450 mμ and an end absorption at longer wavelength were also observed. On the THF and dioxane solutions the absorptions were observed at 520 and 535 mμ respectively, shifting

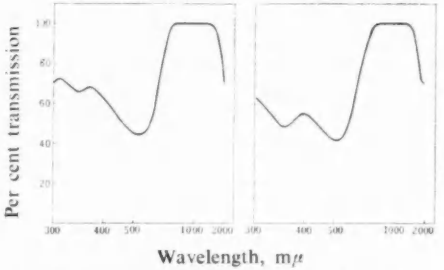


Fig. 2. Spectrum of the toluene solution of the living polymer of styrene.

Fig. 3. Spectrum of the THF solution of benzyl anion sodium.

toward longer wavelength according as the solutions were diluted.

The near infrared spectrum for the filmy state of the living polymer of styrene from 2 to 3.5 μ was the same as that of polystyrene, but its intensity was stronger than that of "dead polymer"* throughout this region. Therefore a very broad absorption in this region may exist. In the cases of the living polymers of styrene with potassium, rubidium and cesium in toluene solution, the corresponding absorptions were observed at 518, 525 and 535 mμ respectively.

For the living polymer of 1, 1-diphenyl ethylene in THF solution, the absorption at 525 mμ and two other absorption at 450 mμ and the end one at longer wavelength were also observed.

In cases of α-methyl styrene and p-methyl styrene of toluene solution the absorption at 515 mμ was observed in addition to two other absorptions.

The absorptions at 550 and 1650 mμ were observed in case of divinyl benzene, and the latter seems to correspond to the end absorptions at longer wavelength for the living polymers of styrene etc.

A spectrum of the red THF solution of alkali benzyl is shown in Fig. 3. A maximum absorption which is characteristic of alkali benzyl at 505 mμ was observed in addition to two other absorptions. The shift of the maximum absorption at 505 mμ which originated from the alteration of alkali metal was very small. This absorption obeyed the law of Beer-Lambert within a concentration range of $10^{-2}\sim10^{-3}$ moles per litre.

Isoprene and butadiene reacted with sodium film, forming yellow adducts of high molecular weight. Dissolving these adducts into THF, slightly yellow and very reactive solutions were obtained. These solutions showed the maximum absorptions at 375 and 357 mμ respectively, and could initiate the polymerization of styrene and isoprene. These absorptions quickly disappeared upon exposure to air. A spectrum for the living polymer of isoprene in THF solution is shown in Fig. 4.

A yellow solution of allyl sodium containing sodium allylate, which was a byproduct[9] of the reaction, had a maximum absorption at 375 mμ and an end absorption at longer wavelength as shown in Fig. 5. The maximum absorption at 375 mμ was unaltered on dilution within the concentration range of $10^{-2}\sim10^{-3}$ moles per litre.

* The reaction product of the living polymer with air, and such product has no more reactivity to initiate the polymerization of styrene etc.

9) R. L. Letsinger and J. G. Traynham, *J. Am. Chem. Soc.*, **70**, 3342 (1948).

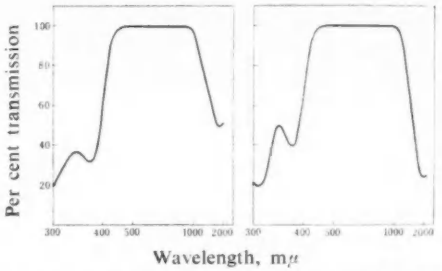


Fig. 4. Spectrum of the THF solution of the living polymer of isoprene.

Fig. 5. Spectrum of the THF solution of allyl sodium.

Block polymerization of isoprene with styrene was carried out, by use of the living polymer of styrene as the initiator, as follows: A constant amount of purified isoprene monomer was added by distillation through a breakable joint into the THF solution of styrene living polymer contained in ampoul D (Fig. 1). The absorption at 510 mμ of the living polymer of styrene (Fig. 6a) decreased by addition of isoprene and the absorption at 375 mμ of the living polymer of isoprene appeared as shown in Fig. 6b. The latter increased by further addition of isoprene as shown in Fig. 6c.

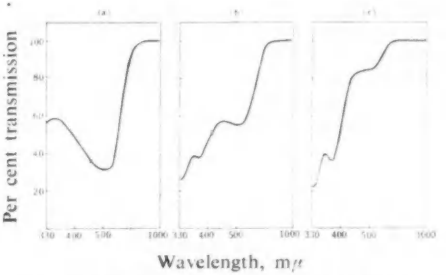


Fig. 6. Change of spectrum in the block polymerization of isoprene by the living polymer of styrene.

Discussion

Absorption Spectra of Benzyl Anion Type. — Since the two maximum absorptions and the end absorption observed for the living polymer of styrene disappeared quickly upon exposure to air, they seem to be characteristic of the living polymer. However, when the starting materials used were not perfectly purified, yellow solutions were obtained. They had the maximum absorption only at 430 mμ besides the end absorption, and could not initiate polymerization. These two absorptions, therefore, may have originated from the decomposition product of the living polymer.

It seems that the temperature dependence of the absorption at 510 mμ of the living polymer of styrene may indicate the behaviour of association, but further study is necessary to confirm the conjecture.

The other absorption at 510 mμ, which may be a characteristic measure of the living polymer of styrene varied according as the kind of alkali metal was altered. The intermolecular charge-transfer spectra shown by a large number of molecular complexes in solution were found to exhibit certain regularities in regard to wavelength[10]. The wavelength of these transitions shows an excellent correlation i.e. a linear relation between frequency ν and ionization potential I_p of the electron donor partners of the complexes:

$$h\nu = 0.61 I_p - 1.8 \text{ (in eV.)}$$

In case of the living polymer of styrene, the similar relation seems to exist as shown in Fig. 7, but the decrease of wavelength with the increase of ionization potential was small as compared with those of the molecular complexes, and also no donor-acceptor complexes such as a type containing alkali metal as the donor or aromatic hydrocarbon as the acceptor has been known. The change of absorption, therefore, would be caused by the change of solvation or dissociation of the polymer anion.

Considering the facts that the position of the maximum absorption near 505 mμ of THF solution of benzyl sodium is constant on dilution and that ether solution of benzyl sodium is conductive as shown by previous investigators[11], it is believed that alkali benzyl

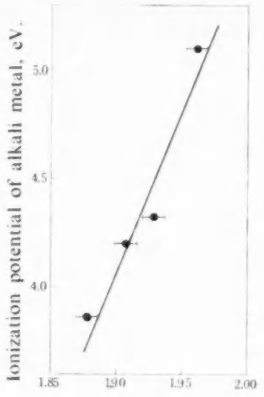


Fig. 7. Ionization potential of alkali metal versus the frequency of the absorption maximum.

in dilute THF solution is completely ionized. The absorption curve of alkali benzyl is the same as that of the living polymer of styrene. It seems evident, therefore, that the end group of benzyl anion type exists in the solution.

The theoretical investigations on the electronic states of benzyl anion and allyl anion were already carried out by several researchers[12-14]. Theoretically calculated wavelength of absorption for benzyl anion, shown in Table I are shorter than that of the observed absorption. The cause of this difference is partly due to the solvation of anion, but this effect may not be so much. Therefore,

Table I. Maximum absorption of the living polymers, alkali benzyl and allyl sodium

	Living polymer of styrene with sodium	Alkali benzyl			Living polymer of butadiene with sodium	Living polymer of isoprene with sodium	Allyl sodium
		Sodium	Potassium	Rubidium			
Wavelength(mμ) obs.	510(530)	510	512	515	357	375	375
Wavelength(mμ) theor.	464 (transition $^1A_1-{}^1B_1$)[b]				326[c], 250[a,c] (transition $^1A_1-{}^1B_1$)		
Extinction coeff. obs.	1.9×10^4	—	—	—	—	3.2×10^2	
Oscilator strength theor.	0.43				0.036		

a) Chalvet[16], b) Longuet-Higgins and Pople[15], c) corrected value.

Table II. Maximum absorptions of the living polymers of styrene and its derivatives

	Styrene	α-Methyl styrene	p-Methyl styrene	Divinyl benzene	1,1-Diphenyl ethylene
Wavelength(mμ) (λ) obs.	510($=\lambda_s$)	515	515	550	525
λ/λ_s obs.	1.00	1.01	1.01	1.08	1.03
λ/λ_s theor.	1.00	1.01	1.01	1.04	1.00

10) H. McConnell, J. S. Ham and J. R. Platt, *J. Chem. Phys.*, **21**, 66 (1953).
11) W. Schlenk, *Ber.*, **50**, 262 (1917).
12) W. Bingel, *Z. für Naturforschung*, **10a**, 463 (1955).
13) H. G. Longuet-Higgins and J. A. Pople, *Proc. Phys. Soc., (London)*, **A68**, 591 (1955).
14) O. Chalvet, *Comt. rend.*, **234**, 2369 (1952).

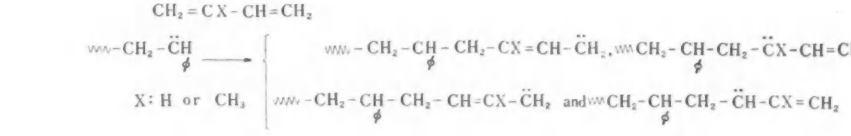
it may be attributed to oversimplification of the theory or to inadequate estimation of the electron interaction integrals used, as will be discussed later in the case of allyl anion.

The small difference of the absorption maximum between the solution of alkali benzyl and the living polymer of styrene may be ascribed to the effect of substitution of α-hydrogen of benzyl anion by the polymer chain of polystyrene, since no difference was observed between the solution of alkali benzyl-polystyrene mixture and that of alkali benzyl.

As an effect of substitutions in anionic group of the living polymer of styrene, it was observed that the maximum absorption shifted toward a longer wavelength as the π-electronic conjugation in anionic group became larger. This effect was approximately interpreted by the Hückel treatment on the π-electronic structure of the anions as shown in Table II.

Absorption Spectra of Allyl Anion Type.—By comparing the maximum absorptions of the living polymers of butadiene and isoprene at 375 and 357 mμ with that of allyl sodium, they seem to be characteristic of allyl anion. Extinction coefficient of the absorption for the living polymer of isoprene was the order of 3×10^3 corresponding to the calculated oscillator strength of the order of 0.036 for allyl anion. Two other absorptions for the solution of the living polymers and that of anion may be attributed to the decomposition product or the byproduct. A typical value[14] of the longest wavelength calculated semi-empirically for allyl anion is shown in Table I, where considerable discrepancies between calculated and experimental values exist. This may be ascribed to the solvation of the anion in solution to some extent, but should rather be attributed to other causes: for example, rough approximation in the theory or inadequate estimation of the integrals used. If the Coulomb electronic repulsion integral for the two electrons on adjacent two carbon atoms in the method of Pople or of Pariser and Parr is decreased, a better approach to the observed value will be obtained*. Such a correction seems to be reasonable since the abnormally partial distribution of electronic charge, which resulted from the calculation, diminishes at the same time. A value corrected on this line is listed in Table I, showing that the partial distribution of charge diminishes to that of the Hückel method. It may be reasonable to consider that the structure of the living polymers of butadiene and isoprene are the polymer anion having the group of allyl anion type at the end of a polymer chain.

Both benzyl sodium and allyl sodium were known to have a reactivity as the initiators of polymerization of styrene[15] etc. Therefore, it may be plausible to attribute the reactivity of the living polymers to their anionic groups. Such a presumption was justified by the change of spectrum for the living polymer of styrene to that for isoprene, in the block polymerization of isoprene by the use of the living polymer of styrene as the initiator; the alteration of end group of benzyl anion type with that of allyl anion type may occur as follows:



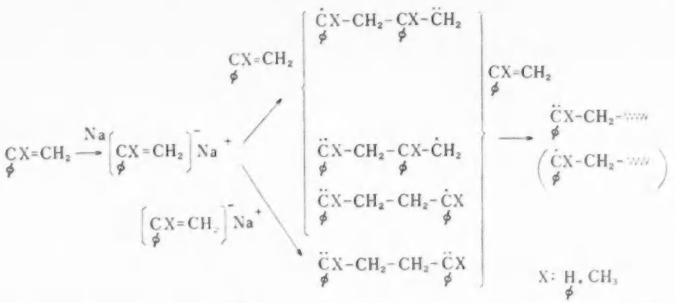
Mechanism of Polymerization.—The existence of the radical anion of styrene and its derivatives in the living polymers of low molecular weight was shown by the paramagnetic resonance absorption measurements[6,17]. Then the first step of the polymerization of styrene and its derivatives may be the formation of the radical anion which can play the role of the initiator of polymerization. The next step is the successive addition of monomers to the radical anion which will convert into the polymer anion making the polymerization reaction proceed. The end groups of radical type did not remain in the solution of the living polymers except the relatively stable diphenylmethyl radical type formed from the radical anion of 1, 1-diphenyl ethylene[16,17]. The general reaction scheme may be as follows:

* Since the electronegativities of the carbon atoms of the anions should be different from these of the neutral molecule, the correction on this line is also necessary.

15) A. A. Morton, *J. Am. Chem. Soc.*, **68**, 93 (1946).

16) K. Kuwata, K. Morigaki, K. Hirota and J. Itoh, *Annual Reports of the Institute for Fibre Research (Sen-i Kagaku Kenkyu-jo Nen-po)*, **12**, 9 (1959).

17) K. Kuwata, S. Ishida and K. Hirota, *J. Chem. Soc. Japan Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **80**, 25 (1959).



This scheme is more general than that of Szwarc, because the formation of radical anions is considered in addition to the bivalent dimer anion proposed by Szwarc.

In cases of butadiene and isoprene the situation is the same, but the existence of monomer radical anion has been confirmed experimentally only with isoprene[18].

Summary

The absorption spectra of the living polymers of styrene and its derivatives as well as of alkali benzyl have been measured from near infrared region to near ultra violet region, and they were compared. It has been concluded that these living polymers are the polymer anions having the groups of benzyl anion type at the end of a polymer chain.

The living polymers of butadiene and isoprene have been separated as the intermediates of polymerization by metallic sodium, and their spectra have been measured. Comparing these spectra with that of allyl sodium, it has been concluded that the living polymer of butadiene and isoprene are the polymer anions having the groups of allyl anion type at the end of a polymer chain. The spectroscopic study on the block polymerization of isoprene with the living polymer of styrene has been carried out. The mechanism of polymerization has been discussed.

The author wishes to express his sincere thanks to Professor Kozo Hirota of Osaka University for his guidance and encouragement throughout this work, and is also indebted to Professor Saburo Nagakura of Tokyo University for his helpful discussions.

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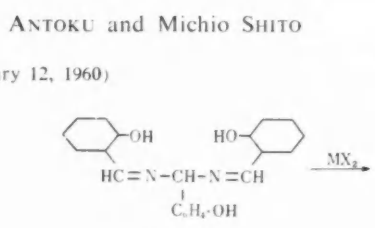
18) K. Kuwata, K. Morigaki and K. Hirota, This Bulletin, 32, 895 (1959).

Coördinate Valency Rings. XXIV.[1] *On Some Inner Complex Ferric Salts of Hydrosalicylamide and its Derivatives**

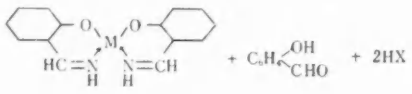
By Tokuichi TSUMAKI, Shigetoshi ANTOKU and Michio SHITO

(Received February 12, 1960)

It is well known that salicylaldehyde reacts readily with ammonia in an alcoholic solution to form hydrosalicylamide, which consists of 3 molecules of salicylaldehyde and 2 molecules of ammonia, involving elimination of 3 molecules of water. When hydrosalicylamide is treated with divalent metallic salts, such as



hydrosalicylamide



(1)

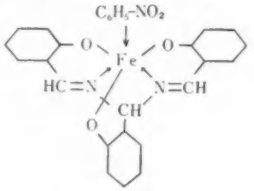
1) Part XXIII: T. Tsumaki, K. Katsuta and S. Okada, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), 78, 1086 (1957).

* Presented at the Joint Meeting of the Chugoku-Shikoku Branch and Kyushu Branch of the Chemical Society of Japan, Matsuyama, June 7, 1958.

copper or nickel salts, metal chelates of salicylaldimine (formula 1) instead of those of hydrosalicylamide are obtained[2].

In the chelate-forming reactions, therefore, hydrosalicylamide splits by metallic salts giving one molecule of salicylaldehyde.

An attempt was made in 1934, by one of the authors[3], to obtain an analogous ferrous complex salt, that is, bis-salicylaldimine-iron-(II) by the reaction between hydrosalicylamide and ferrous sulfate. But the obtained chelate recrystallized from nitrobenzene was trisalicylaldehyde-diimine-iron(III), which contained one molecule of nitrobenzene coördinated to iron atom (formula 2). During the reaction, therefore, ferrous complex salt was oxidized to ferric by atmospheric oxygen.



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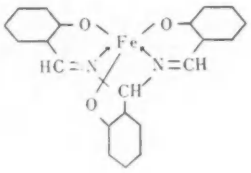

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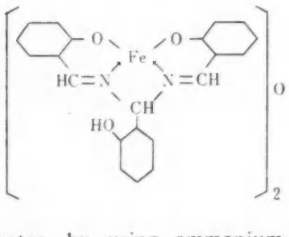


(4)

Later, by using ammonium ferric sulfate, instead of ferrous sulfate, the same product was obtained as had been expected[4].

In the above-mentioned reactions, the main product, before recrystallization from nitrobenzene, consists of reddish brown powder. In the present paper are described the method of preparation of this compound in pure state and the comfirmation of its chemical structure. The structure of the compound, in recognition of the structure of nitrobenzene-containing chelate indicated by formula 2, is considered as a rarely known penta-coördinated ferric complex (formula 3). Besides formula 3, another formula, 4, may be taken into consideration for the ferric complex, on the basis of the results of elementary analysis and of the route of preparation of the complex. Of these two formulae, the latter should be excluded for reasons described below.

1) The complex salt does not react with diazomethane. The presence of a phenolic hydroxyl group must be denied.

2) It is known that the ferric complexes of oxide-form, for example, bis-salicylaldehyde-ethylenediimine-ferric oxide, react with a number of weak organic acids to give their salts (formula 5)[5]. Our complex, however, does not show such behavior.

3) If the hydroxyl group of the central salicylidene group does not take part in the complex formation as in the case of formula 4, the synthesis of a complex salt having formula 6, which has a benzylidene group in place of a salicylidene group in formula 4, may be possible by the action of a ferric salt on 2, 2′-dihydroxyhydrobenzamide. The complex salt of formula 6, however, could not be obtained by such attempts, and only a complex salt of hydrosalicylamide having formula 3 was obtained. Therefore, it can be considered that benzaldehyde splits off from the ligand and salicylaldehyde takes its place in the course of the reaction. This fact indicates that three hydroxyl groups of hydrosalicylamide may all be used for the complex formation.

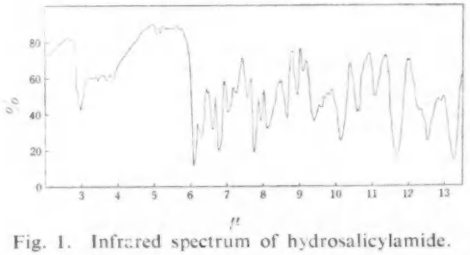


Fig. 1. Infrared spectrum of hydrosalicylamide.

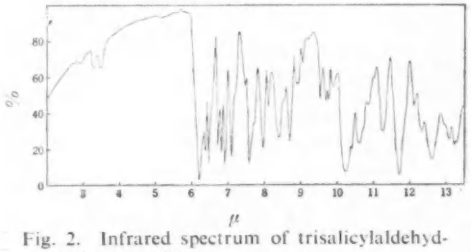


Fig. 2. Infrared spectrum of trisalicylaldehyd-diimine-iron(III).

2) P. Pfeiffer, E. Buchholz and O. Bauer, *J. prakt. Chem.*, **129**, 163 (1931).

3) T. Tsumaki, *J. Chem. Soc. Japan (Nippon Kwagaku Kwaishi)*, **55**, 1245 (1934).

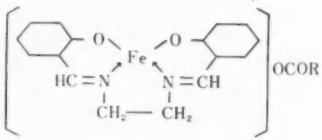
4) T. Tsumaki, ibid., **56**, 1329 (1935).

5) P. Pfeiffer, E. Breith, E. Lübbe and T. Tsumaki, *Ann.* **503**, 84 (1933). T. Tsumaki, M. Kuramoto, Y. Nakaishi and S. Suzuki, *Reports of Faculty of Science, Kyushu Univ., Chem. Sec.*, **1**, 63 (1950).

4) The infrared spectra indicate the absence of phenolic hydroxyl groups (Figs. 1 and 2).

Because of the above-mentioned experimental facts, the pentadentate formula 3 should be given to the ferric complex in question and the structure (formula 2) of its nitrobenzene-containing adduct has been proved to be correct.

For some of the so-called tri-coördinated copper complexes, the presence of dimeric molecules has been suggested because of their abnormally low magnetic moments[6]. In the case of our pentadentate ferric complex, it has been shown by the measurement of magnetic susceptibilities that it has a normal magnetic moment (5.82 B. M.) and O–Fe bonds are essentially ionic. Therefore, the complex does not exist in the form of dimers.



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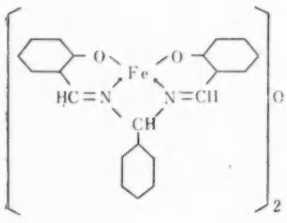

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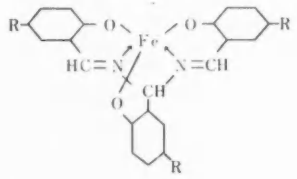

(7)

As the penta-coördinated complex is coördinatively unsaturated, it will be expected that the complex will have a strong tendency to become a hexa-coördinated one, by the addition of a ligand molecule. The nitrobenzene adduct is a good example. Further, we succeeded in obtaining some such adducts, which contain pyridine, quinoline, bromobenzene, α-chloronaphthalene, ethylene chloride and methyl benzoate. Each of the ligand molecules, except ethylene chloride, is bound firmly to the complex. The expelling of them is completed only by heating the adducts at 150~170°C for 8~10 hr. under 10 mmHg. It is well known that tertiary amines such as pyridine or quinoline enter very often into the complexes as ligands, but the examples of adducts which contain nitro-compounds or halogenated hydrocarbons have been rarely known.

Starting from benzene-substituted methyl-, chloro-, bromo- and nitro-derivatives of hydrosalicylamide, corresponding penta-coördinated iron complexes and their hexa-coödinated adducts were obtained (formula 7). In the case of methyl derivative, however, it formed no addition compound.

All these complexes decompose hydrogen peroxide catalytically and for that reason show strong chemi-luminescence in the presence of luminol in an alkaline solution.

Experimental

Trisalicylaldehyde - diimine - iron(III). — Hydrosalicylamide (2 g.) is dissolved in absolute alcohol (300 cc.) in a three necked round-bottomed flask (500 cc.) fitted with a glass filter, a stirrer and a reflux condenser protected by calcium chloride. The solution is stirred and heated to 70~75°C on a water bath. A solution of anhydrous ferric chloride (0.6 g.) in absolute alcohol (50 cc.) is allowed to flow into the flask through a glass filter. The solution changes at once from yellow to orange red. After about two hours the reaction product is filtered off, washed with hot alcohol several times and dried at 90°C. Yield 1.5 g., black needles.

Found: C, 62.71; H, 4.18; N, 6.76; Fe, 13.78. Calcd. for $C_{21}H_{15}N_2O_3Fe$: C, 63.18; H, 3.78; N, 7.02; Fe, 13.99%.

Reaction between 2,2'-Dihydroxyhydrobenzamide and Ferric Chloride.—The reaction is carried out by essentially the same method as described above, using 2,2'-dihydroxyhydrobenzamide and ferric chloride. The resulting black crystals are recrystallized from nitrobenzene.

Found: N, 8.25; Fe, 10.52; drying loss, 23.66. Calcd. for $C_{21}H_{15}N_2O_3Fe \cdot C_6H_5NO_2$: N, 8.05; Fe, 10.69; nitrobenzene, 23.57%.

Since the description in the literature regarding 2,2'-dihydroxyhydrobenzamide had been only briefly given in the U. S. patent[7], a sample synthesized by the authors was ascertained by elementary analysis. m. p. 117°C. Pale yellow needles.

Found: C, 76.48; H, 5.52; N, 8.35. Calcd. for $C_{21}H_{15}N_2O_2$: C, 76.34; H, 5.49; N, 8.48%.

Magnetic Susceptibility.—The magnetic susceptibilities of trisalicylaldehyde-diimine-iron(III) and its nitrobenzene adduct were measured by the Curie method at room temperature (17°C). Cupric sulfate pentahydrate (further purified by the recrystallization of an extra pure reagent thrice from water) was used as the standard sample. The results are presented in Table I, where χ is the magnetic susceptibility per gram of the complex.

Neglecting the diamagnetic contribution of the ligand and assuming the validity of Curie-Langevin's law, the effective magnetic moments μ per one mole of the complex were calculated (see also Table I).

6) M. Kishita, Y. Muto and M. Kubo, *Austral. J. Chem.*, **10**, 386 (1957).
7) J. A. Chenicek, U. S. Pat. 2,533,205 (1950).

TABLE I.

	χ (c. g. s., e. m. u.)	μ' (B. M.)
Trisalicylaldehyde-diimine-iron(III) + nitrobenzene	28.5×10^{-6}	5.90
Trisalicylaldehyde-diimine-iron(III)	36.3×10^{-6}	5.82

The theoretical moment of iron(III) (calculated from "spin-only" formula) is 1.73 B. M. for covalent bonds and 5.92 for the ionic ones.

Infrared Spectra.—They were taken in a hexachlorobutadiene mull, with an Oyo-Koken double beam instrument equipped with a sodium chloride prism (Figs. 1 and 2).

Addition Compounds of Trisalicylaldehyde-diimine-iron(III).—These compounds were prepared by the recrystallization of trisalicylaldehyde-diimine-iron (III) from various organic solvents. They are dried in a vacuum desiccator, because the coördinated solvent molecules are partially removed on heating or by washing with alcohol. All of them form black plates and their appearance or colors are almost unaltered by desolvation.

Trisalicylaldehyde-diimine-iron(III)+Pyridine.

Found: N, 8.88; Fe, 11.51; drying loss, 16.90. Calcd. for $C_{21}H_{15}N_2O_3Fe\cdot C_5H_5N$: N, 8.79; Fe, 11.68; pyridine, 16.54%.

Trisalicylaldehyde-diimine-iron(III)+Quinoline.

Found: C, 67.94; H, 4.46; N, 7.82; Fe, 10.42; drying loss, 24.63. Calcd. for $C_{21}H_{15}N_2O_3Fe\cdot C_9H_7N$: C, 68.18; H, 4.17; N, 7.95; Fe, 10.57; quinoline, 24.43%.

Trisalicylaldehyde-diimine-iron(III)+α-Chloronaphthalene.

Found: C, 65.95; H, 4.26; N, 4.78; Fe, 9.60. Calcd. for $C_{21}H_{15}N_2O_3Fe\cdot C_{10}H_7Cl$: C, 66.27; H, 3.95; N, 4.99; Fe, 9.33%.

Trisalicylaldehyde-diimine-iron(III)+Ethylene Chloride.

Found: C, 57.35; H, 4.13; N, 5.72; Cl, 12.35; Fe, 11.65; drying loss, 16.40. Calcd. for $C_{21}H_{15}N_2O_3Fe\cdot0.8\ C_2H_4Cl_2$: C, 57.12; H, 3.86; N, 5.90; Cl, 11.94; ethylene chloride, 16.00%. The complex salt desolvates at room temperature. The analytical results shown above are the average values of several analyses.

Trisalicylaldehyde-diimine-iron(III)+Methyl Benzoate.

Found: Fe, 10.32; drying loss, 25.92. Calcd. for $C_{21}H_{15}N_2O_3Fe\cdot C_8H_8O_2$: Fe, 10.43; methyl benzoate, 25.43%.

Tri(5-substituted-salicylaldehyde)-diimine-iron-(III).

Tri(5-methylsalicylaldehyde)-diimine-iron(III).—By a method similar to that mentioned above for the synthesis of trisalicylaldehyde-diimine-iron(III), a solution of ferric chloride (0.4 g.) in absolute alcohol (10 cc.) is added to a solution of 5, 5', 5''-trimethylhydrosalicylamide (1 g.) in absolute alcohol (70 cc.). But in this case, in order to avoid the decomposition of the ligand at high temperature, the reaction is carried out at 45~50°C. The product was purified by reprecipitation from pyridine with water. Black needles.

Found: C, 64.87; H, 4.98; N, 6.36; Fe, 12.40. Calcd. for $C_{24}H_{21}N_2O_3Fe$: C, 65.32; H, 4.80; N, 6.35; Fe, 12.66%.

Tri(5-bromosalicylaldehyde)-diimine-iron(III)+Nitrobenzene.—A solution of 5, 5', 5''-tribromohydrosalicylamide (1 g.) (or 5-bromosalicyladehyde and ammonia) in alcohol (30 cc.) is warmed on a water bath and a solution of ammonium ferric sulfate (dodecahydrate; 0.7 g.) in water (7 cc.) is added to it. After about half an hour, the black brown precipitates are filtered off, washed with hot alcohol and dried on a tone plate. Yield 0.7 g.

The powder is recrystallized from nitrobenzene to give the black plates which are dried in vacuo.

Found: C, 42.87; H, 2.48; N, 5.37; Fe, 7.27; drying loss, 16.17. Calcd. for $C_{21}H_{12}N_2O_3Br_3Fe\cdot C_6H_5NO_2$: C, 42.67; H, 2.25; N, 5.37; Fe, 7.36; nitrobenzene, 16.20%.

Tri(5-bromosalicylaldehyde)-diimine-iron(III)+Bromobenzene.—The black brown powder obtained above is recrystallized from bromobenzene. Dark violet needles.

Found: N, 3.64; Fe, 6.90; drying loss, 19.81. Calcd. for $C_{21}H_{12}N_2O_3Br_3Fe\cdot C_6H_5Br$: N, 3.54; Fe, 7.05; bromobenzene, 19.81%.

Tri(5-chlorosalicylaldehyde)-diimine-iron(III)+Nitrobenzene.—The reddish brown powder is obtained by the same treatment as in the case of the bromoderivative, using a solution of 5, 5', 5''-trichlorohydrosalicylamide (3.5 g.) (or 5-chlorosalicylaldehyde and ammonia) in alcohol (60 cc.) and a solution of ammonium ferric sulfate (dodecahydrate; 4 g.) in water (20 cc.). Yield 3 g. This powder is recrystallized from nitrobenzene. Black plates.

Found: N, 6.88; Fe, 9.05; drying loss, 19.49. Calcd. for $C_{21}H_{12}N_2O_3Cl_3Fe\cdot C_6H_5NO_2$: N, 6.72; Fe, 8.93; nitrobenzene, 19.67%.

Tri(5-chlorosalicylaldehyde)-diimine-iron(III)+Bromobenzene.—This is prepared by the recrystallization of the powder from bromobenzene. Dark violet needles.

Found: N, 4.01; Fe, 8.64; drying loss, 23.55. Calcd. for $C_{21}H_{12}N_2O_3Cl_3Fe\cdot C_6H_5Br$: N, 4.24; Fe, 8.47; bromobenzene, 23.80%.

Tri(5-nitrosalicylaldehyde)-diimine-iron(III)+Nitrobenzene.—A Solution of 5, 5', 5''-trinitrohydrosalicylamide (1 g.) in alcohol (50 cc.) is warmed on a water bath and a solution of ammonium ferric sulfate (dodecahydrate: 0.7 g.) in water (10 cc.) is added to it. The resulting reddish brown precipitates are treated as before. This powder is insoluble in common organic solvents and slightly soluble in nitrobenzene. When the powder is recrystallized from nitrobenzene, a small amount of crystals is obtained after about two days.

Found: N, 12.41; Fe, 8.43; drying loss, 18.48. Calcd. for $C_{21}H_{12}N_5O_9Fe\cdot C_6H_5NO_2$: N, 12.79; Fe, 8.50; nitrobenzene, 18.70%.

The authors wish to express their thanks to Miss S. Indo for N-analysis, to Dr. K. Hirakawa (Department of Physics) for the measurement

of magnetic susceptibilities, and to Assistant Professor Dr. Y. Ueda, Dr. H. Yoshimura and Mr. H. Yano (Department of Pharmacy, Faculty of Medicine) who kindly took the infrared spectra.

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*Studies on Leucomycin. II. Preparative Chromatography of Macrolides on Amberlite IRC-50**

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As shown in the previous paper[1], leucomycin, a basic antibiotic produced by *Streptomyces kitasatoensis* Hata[2-4], was proved by the paper-chromatographic and -electrophoretic analysis, to be a mixture composed of at least six biologically active components, A_1, A_2, B_1, B_2, B_3 and B_4. Preliminary experiments on the chromatographic separation of these components in a preparative scale showed, that both leucomycin groups, A and B, were able to be absorbed on a column of alumina or silisic acid from the benzene solution and to be separately eluted with the same solvent containing methanol in this order. Using this or similar chromatographic systems, however, recoveries of the antibiotics was markedly low (50~70 per cent in weight, less than 40 per cent in biological activity; presumably accompanied with decomposition) and a more minute resolution into each component, was unsuccessful.

In course of our studies, it was found that leucomycin absorbed on a column of carboxylic resin, such as Amberlite IRC-50 in H-cycle, could be eluted quantitatively with sodium citrate buffer, and that all six components in the leucomycin complex were separately eluted with a mixture of citrate buffer and ethanol, in such a high concentration as the chromatographic system could be used for a preparative separation of these components. Using this method, not only leucomycin complex, but also some derivatives of leucomycin A_1 and other macrolides such as erythromycin[5], magnamycin[6] and spiramycin[7], having dimethylamino sugar as the basic moiety[8], could be purified from the contaminated minor components, which had been separated only with difficulties by counter current distribution. In this paper, we propose to report these results. In addition some properties of purified leucomycin components B_1, B_2, B_3 and B_4 and the composition of these components in leucomycin complex will be reported.

Experimental

Materials.—Leucomycin complex (I)** and the fractionated antibiotics (II, III, IV) were kindly prepared for this study by J. Abe et al., at the Research Institute, Toyo Jozo Co. Ltd., according to the methods summarized in Table I. Erythromycin, magnamycin and spiramycin were the samples furnished as "standard antibiotics" through the National Institute for Preventive Medicine, Tokyo. Diacetylleucomycin A_1 ($C_{50}H_{83}O_{19}N$, m. p. 127~129°C)[9], propionylleucomycin A_1 ($C_{49}H_{85}O_{18}N$, m. p. 123~126°C)[10], tetrahydroleucomycin A_1 ($C_{48}H_{85}O_{17}N$, m. p. 162~164°C)[11], and a basic moiety derived from leucomycin A_1 with the methanolysis ($C_{34}H_{59}O_{13}N$, m. p. 154~155°C; corresponding to carimbose fragment in magnamycin)[12], were prepared from leucomycin A_1 by the present author, according to the methods which will be published soon.

* Pat., Application No. 13908 (1959).

1) J. Abe, Y. Suzuki, T. Watanabe and K. Satake, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 969 (1960).

2) T. Hata, Y. Sano, N. Ohki et al., *J. Antibiotics*, Ser. **A6**, No. 2, 87 (1953).

3) T. Hata, F. Koga and H. Kanamori, *J. Antibiotics*, Ser. **A6** No. 3, 109 (1953).

4) Y. Sano, *J. Antibiotics*, Ser. **A7**, No. 3, 93 (1953).

5) J. M. McGuire, R. L. Bunch, R. C. Anderson, H. E. Boaz et al., *Antibiot. Chemoth.*, **2**, 281 (1952).

6) W. Tanner, A. R. English, T. M. Less and J. B. Routen, *Antibiot. Chemoth.*, **2**, 441 (1952).

7) S. Pinnert-Sindico, L. Ninet, S. Preud'homme and C. Coser, *Antibiot. Annual.*, 724 (**1954**–**1955**).

8) R. K. Darke, *Antibiot. Chemoth.*, **3**, 663 (1953); R. B. Hasbrouck and F. C. Garben, *Antibiot. Chemoth.*, **3**, 1040 (1953); F. A. Hochstein and P. R. Regar, *J. Am. Chem. Soc.*, **77**, 3353 (1955).

** Corresponded to "Commercial bulk".

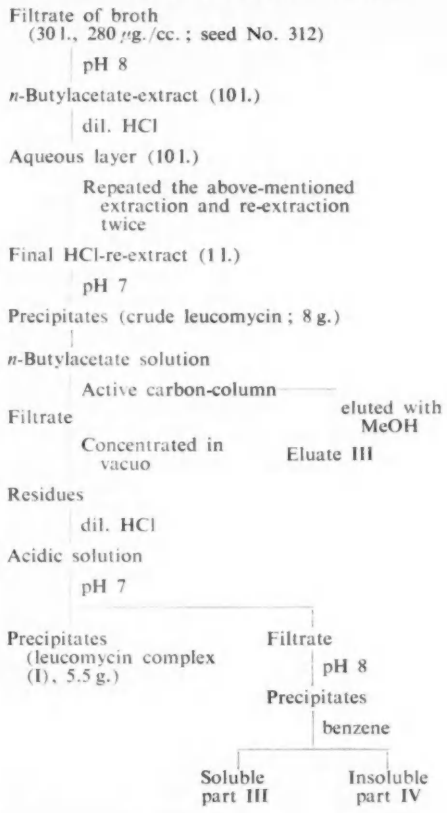
9) C. L. Ogg, W. L. Porter and C. D. Willits, *Ind. Eng. Chem., Anal. Ed.*, **17**, 394 (1945).

10) V. C. Stephens, B. J. S. Conine, *Antibiotic. Annual*, 346 (**1958**–**1959**).

11) T. Watanabe, will be published.

12) R. B. Woodward, *Angew. Chem.*, **68**, 133 (1956).

TABLE I. FRACTIONATION OF LEUCOMYCIN



Chromatography on Amberlite IRC-50.—One hundred grams of the resin (XE-64) of approximately 150 mesh, was suspended in 500 cc. of 1 N sodium hydroxide and the suspensions were heated on a water bath at 60°C for 3 hours under occasional stirring. After the decantation of brown colored supernatant, the resin of the Na-cycle was washed with distilled water thoroughly, then suspended in 1 N hydrochloric acid at room temperature. After 30 minutes, the resin was washed with distilled water until the washing became free from acid. Forty grams of so purified resin of H-cycle, was added as thick suspension in water to a column of 1 cm. in the diameter, to a hight of 45 cm. To the column, 10 mg. of sample to be analyzed was added as 1 per cent solution in N/100 hydrochloric acid. As soon as the applied sample solution had been allowed to flow into the column, washing with 150 ml. of distilled water, then elution with a mixture of 96 per cent ethanol and M/5 sodium citrate buffer (Na^+ 1.6 g. ion per liter, pH 5.0) in an equal volume, was initiated at a flow rate of 9 cc. per cm^2 per hour at 15°C. The effluent was collected in 4.5 cc. fraction by means of automatic fraction collector. For the chromatography in a preparative scale (15 g. of sample), a column of 3×180 cm. was used.

Chemical Assay of Leucomycin in the Effluent.—The concentration of leucomycin in each effluent fraction was determined photocolorimetrically with sulfuric acid as follows. An aliquot of sample solution was mixed with an equal volume of concentrated sulfuric acid under adequate shaking, and the resulting red brown color was measured between 10 and 30 minutes after the addition of sulfuric acid, with Kotaki photometer Model D2 using filter 470. Experiments showed, that the readings were strictly proportional to leucomycin concentration up to an optical density of about 1.1 equivalent to approximately 500 γg per cc. of leucomycin complex (I) and they were not affected by the presence or absence of M/5 citrate and of 50 per cent ethanol. As the color developed per unit weight of leucomycin components, were not just the same, the correction was made for the calculation of weight composition of each component. This method could be also applied with success for the assay of leucomycin derivatives and other macrolides, except erythromycin which with sulfuric acid colored only slightly. The fact, however, did not prevent the determination of an approximate elution position of erythromycin with this coloration.

Paper Chromatography of Leucomycin.—Leucomycin components contained in each fraction of chromatographic effluent, were identified from the chromatographic R_f values, A and B groups could be easily distinguished from the R_f developed with *n*-butyl acetate containing M/15 sodium phosphate (pH 6); while A_1 and A_2; B_1, B_2, B_3 and B_4 from the R_f developed with M/15 sodium phosphate containing *n*-butyl acetate (pH 8) on a liquid paraffin-treated filter paper. The position of the leucomycin component migrated on the filter paper, was detected as a growth-inhibited zone of *Bacillus subtilis* on the bioautogram[1].

Isolation of Leucomycin Components.—Fractions corresponding to each peak on the elution diagram, were combined and cocentrated to about one third volume under reduced pressure. The basic antibiotics in the aqueous concentrates, after adjusting the pH to 8, were extracted with *n*-butyl acetate. From the acid re-extract of the ester layer, leucomycin was crystallized by adjusting the pH to 7. For the recrystallization benzene-cyclohexane solvent for A group and hot benzene for the B group were used.

Assay of Antibacterial Activity.—The assay of the antibacterial activity of the so purified components, was kindly done by the Bioassay Division, Toyo Jozo Co. Ltd., according to the usual cup method against *Bacillus subtilis* No. 209 as the test organism.

Results

Chromatography of Leucomycin.—Fig. 1-A represents a typical elution diagram of a leucomycin complex (I) from a column of Amberlite XE-64 (H-cycle) with a mixture of ethanol and M/5 sodium citrate buffer (pH 5.0) in an equal volume. Fig. 1-B illustrates the paper-chromatograms of the above-mentioned effluent fractions detected by the growth-inhibition of

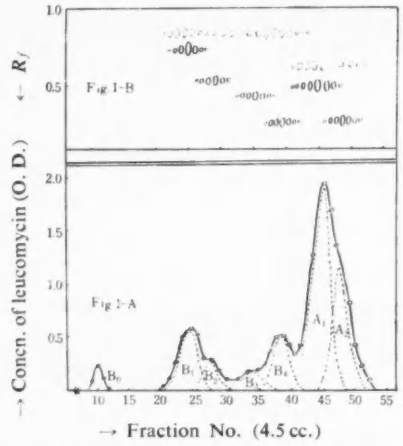


Fig. 1-A. Chromatography of leucomycin complex (I) on 1×40 cm. column of Amberlite XE-64, eluted with a mixture of 96 per cent ethanol and M/5 citrate buffer in an equal valume, at a flow rate of 9 cc. per cm^2 per hour at 15°C. -⊙- concentration (uncorr.) assayed photocolorimetrically. ---- concentration of each component presumed from paper chromatographic analysis (Fig. 1-B).

Fig. 1-B. Composite paper chromatograms of each effluent fraction. ◌ developed with *n*-butyl acetate containing phosphate buffer (pH 6). ○ developed with phosphate buffer (pH 8) containing *n*-butyl acetate.

Bacillus sabtilis. These results indicated that leucomycin components, B_1, B_2, B_3, B_4, A_1 and A_2 were eluted from the column in this order and these components could be separated from each other under the conditions used, except the last two components A_1 and A_2, which could be only partially separated***. A minor component B_0 eluted at the hold-up volume, colored with concentrated sulfuric acid but showed no antibacterial activity (less than 10 unit per mg.). Some discrepancies occasionally observed between both of the amounts of leucomycin complexes, assayed photocolorimetrically and biologically, might be due in part to the presence of this component. The recovery of leucomycin from the column assayed both photocolorimetrically and biologically, was more than 90 per cent and the rechromatography of each component showed an elution of only one component at the same position, indicating that no appreciable degradation occurred for this antibiotic.

*** Recently, however, both of the components were found to be completely separated on a longer column (1.5~2.0 m.), if the amount of the sample added to the column was limited.

The reproducibility of this chromatography was fairly good and the position of the elution of each component varied only within 5 per cent, so far as the chromatographic conditions mentioned rather in detail in the experimental part were exactly maintained. The flow rate of 9 cc./cm^2/hr. seemed to be an upper limit for the elution without any broadening of each peak. The pH of buffer should be selected between 4 and 8, as the more acidic or alkaline pH caused slight degradation of leucomycin even at room temperature. In this region, the higher the pH, the less the spreading of the elution peak but also lesser than the separation of the components among each other. Most important in this chromatographic method is the temperature. At higher temperature than 25°C, all components were eluted very rapidly, while at a lower than 10°C very slowly, and both of the extremes resulted into a poor resolution. For a precise analysis, a device to maintain the temperature of the column at a constant (15~20°C) might be profitable.

Leucomycin Components.—From the elution diagram as shown in Fig. 1, the composition of the leucomycin complex (I) was estimated to be composed of 11 per cent of B_1, 7 per cent of B_2, 8 per cent of B_3, 13 per cent of B_4, 32 per cent of A_1 and 24 per cent of A_2, in weight respectively. These values were by no means inconsistent with those estimated from the counter current distribution diagram of the same sample[13].

Using the same chromatographic technique, another sample of leucomycin complex (I) produced by a new strain (seed No. L 149-373) and some fractionated leucomycin samples (II, III and IV) from the original strain, were analyzed. The results indicated, that a new strain of *Streptmyces kitasatoensis* produced mainly A components; B components produced by the original strain were much more absorbed on a column of active carbon from the *n*-butyl acetate solution and were precipitated at higher pH from the aqueous solution than A components did; and the crystallization of B components from benzene was effective for the separation of B_2 and B_4 from less active components B_1 and B_3. Four leucomycin components, B_1, B_2, B_3 and B_4 and partially purified A_1 (contaminated small amount of A_2) were actually isolated from the preparations which had been previously fractionated (see Table I) according to the above mentioned method by the use of preparative column (3×180 cm.).

The antibacterial activity of A_1, though still contaminated with a small amount of A_2, was as much as 1000 unit per mg. This value was

13) T. Watanabe, H. Nishida, J. Abe and K. Satake, This Bulletin, 33, 347 (1960).

TABLE II. YIELDS, PROPERTIES AND ANTIBACTERIAL ACTIVITY OF LEUCOMYCIN COMPONENTS

Component	Yield (%) from I	II	III	IV	m. p. °C	Molecular formula	Antibacterial activity (unit/mg.)*
A_1	32	12	10	0	132.0~137.0	—	1000
A_2	24	6	3	0	—	—	—
B_0	5	1	0	0	—	—	10
B_1	11	16	53	25	214.5~216.5	$C_{35}H_{59}NO_{13}$	100
B_2	7	28	1	31	214.0~216.0	$C_{35}H_{65}NO_{16}$	215
B_3	8	29	28	12	216.0~217.0	$C_{34}H_{53}NO_{13}$	570
B_4	13	8	5	32	221.0~223.8	$C_{35}H_{59}NO_{16}$	700

* Leucomycin complex (I) ; 560 unit/mg.

approximately 1.8~1.9 times as much as that of leucomycin complex (I) produced by the original strain, and was the highest one as far as known on leucomycin samples. These facts will be explained by the contamination of less active B components. It may be of interest that the activity of B components varied from 700 units to 100 units. According to J. Abe slight undesirable properties observed in the leucomycin complex (produced by the original strain) was mainly due to the presence of B components and their action increased in the following order; B_1, B_3, B_2 and B_4, thus with the decrease of the antibacterial activity. These results are summarized in Table II, together with some analytical data of purified B components.

Chromatography of Leucomycin Derivatives.—Under the same condition as used for the separation of leucomycin complex, some leucomycin derivatives, acetyl-[9], propionyl-[10], tetrahydroleucomycin A_1[11], and a basic moiety derived from A_1 by methanolysis[12], were also eluted quantitatively, but at a different position, which are summarized in Table III. The results indicated that this chromatography was effective for the purification of these derivatives from the unreacted leucomycin A_1. Less-retardation of the basic moiety derived from A_1 by methanolysis and more retardation of the two acyl derivatives on a column of carboxylic acid resin, will be related to their different pK'_a values (pK'_a 5.0 for acyl derivatives; pK'_a 8.1 for basic moiety derived from A_1 by methanolysis) from the original leucomycin A_1 (pK'_a 7.1)****, but the different chromatographic behaviors of A_1 and of the tetrahydro-derivative and of other leucomycin components (pK'_a 6.8~7.1) indicated that " Weiss's effect " would play a predominant rôle in these separations.

Chromatography of Other Macrolides.—Table III lists the elution position of several macrolides, including erythromycin, magnamycin, and spiramycin, from a column of Amberlite XE-64 (H-cycle) with an equi-volume mixture of ethanol and M/5 sodium citrate buffer (pH 5.0). These results, together with the results of the paper-chromatographic and -electrophoretic analysis[1], indicated that all six antibiotics contained in leucomycin complex different from one another well-known macrolides, namely : erythromycin, magnamycin and spiramycin. As reported already by the other authors, antibiotics belonging to macrolides were usually produced as a complex composed of a main and a few minor components, the latter of which could be fairly separated with some difficulties. In these experiments,

TABLE III. THE ELUTION POSITION OF SOME LEUCOMYCIN DERIVATIVES AND MACROLIDES UNDER THE SAME CONDITIONS AS USED FOR THE SEPARATION OF LEUCOMYCIN COMPLEX (I)

Antibiotics			Volume cc.
Leucomycin	Main component	A_1	180~225
	Minor component	B_1	90~120
		B_2	112~144
		B_3	144~166
		B_4	157~189
		A_2	198~238
	Derivatives of A_1	Des-sugar	50~ 76
		Tetrahydro-	71~126
		Acetyl-	201~255
		Propionyl-	197~259
Erythromycin	Main component		126~193
	Minor component		99~144
			189~250
Magnamycin	Main component		76~126
	Minor component		67~ 90
			98~148
Spiramycin	Main component		234~292
	Minor component		126~157
			211~270

**** Basicity of leucomycin is due to the presence of 3-dimethylamino sugar, so the pK'_a was fairly affected by the 2,4-*O*-substitution.

too, some commercial samples of the above-mentioned antibiotics, though considered to be fairly purified, showed the presence of these minor antibiotics. Such minor components of usual macrolides, however, had been limited to only two or three kinds. The presence of many minor components, as much as five in leucomycin seemed to belong to the first case.

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Studies on Leucomycin. III. Isolation[1] *and Properties of Six Antibacterial Components in Leucomycin Complex*

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Leucomycin[2], a basic antibiotic obtained from the broth-filtrate of *Streptomyces kitasatoensis* Hata[3,4], has been presumed to be a macrolides on its physical, chemical[3,5] and antibacterial[3,6] properties. In the previous papers of this series[7,8] it was reported that the antibiotic was a mixture of six biologically active components, A_1, A_2, B_1, B_2, B_3 and B_4 and that the last four minor components, though in a minute amount, could be purified by fractional precipitation[8] of the mixture from aqueous and from benzene solutions (see Table I), followed by the further minute resolution of the resulting fractions by chromatography on a column of Amberlite IRC-50[8]. The main component A_1 which seemed to have the highest activity[8], however, had been scarcely separated from B_1 and another minor component A_2, by this method.

For the resolution of macrolides complex in preparative scale, counter current distribution has been reported to be effective[9-12]. Using this technique, leucomycin complex was also

TABLE I. FRACTIONATION OF LEUCOMYCIN

Filtrate of broth
(30 l. 280 γg./cc.; seed No. 312)
↓ pH 8
n-Butyl acetate extract (10 l.)
↓ dil. HCl
Aqueous layer (10 l.)
→ Repeated the above-mentioned extraction and re-extraction twice
Final HCl extract
↓ pH 7
Precipitates (Crude leucomycin; 8 g.)
↓
n-Butyl acetate solution
↓ active carbon-column
Filtrate → concentrated in vacuo
active carbon-column → eluted with MeOH → Eluate II
Residues
↓ dil. HCl
Acidic solution
↓ pH 7
Precipitate (Leucomycin complex (I), 5.5 g.)
Filtrate
↓ pH 8
Precipitates
↓ Benzene
Soluble part III
Insoluble part IV

1) Japanese Pat., Application No. 13909 (1958).
2) Leucomycin used in this study, was obtained from the broth of *S. kitasatoensis* Hata No. 312, in 1956 and had a similar component composition to that of the original preparation by Hata[3,6]. Recent preparation from No. L-149-373, a mutant of the original strain, was almost free from B components.
3) T. Hata, Y. Sano, M. Ohki, Y. Yokohama A. Matsumae and S. Ito, *J. Antibiotics, Ser.* **A6**, (2), 87 (1953).
4) T. Hata, F. Koga and H. Kanamori, ibid., Ser, A, **6** (3), 109 (1953).
5) Y. Sano, ibid., Ser. A7 (3), 93 (1954).
6) T. Hata, Y. Sano, Y. Yokohama, S. Ito, S. Okazaki, K. Takeno, H. Ito, Y. Owada, Y. Saito and M. Soekawa, ibid., Ser. A6 (4), 163 (1953).
7) J. Abe, Y. Suzuki, T. Watanabe and K. Satake, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 969 (1960).
8) T. Watanabe et al., This Bulletin, **33**, 1100 (1960).
9) J. M. McGuire, L. Bunch, R. C. Anderson, H. E. Boaz, E. H. Flynn, H. M. Powell and T. W. Smith, *Antibiot. Chemoth.* **2**, 281 (1952).
10) R. L. Sagner, F. A. Hochstein and K. Murai, *J. Am. Chem. Soc.*, **75**, 4684 (1953).
11) S. P. Sindico, L. Ninet, S. Preud'homme and C. Coser, *Antibiotics Annual*, 724 (1955-1956).
12) H. Schmitz, M. Misick, B. Heinemann and I. R. Hooper, *Antibiot. Chemoth.*, **7**, 37 (1957).

analyzed[13]. The distribution diagram, though after only 30 transfers, seemed to suggest a partial resolution. These facts prompted us to study the counter current distribution of leucomycin complex (I) (see Table I) in more detail. In this paper we wish to report on these results. In addition, some properties of such purified antibacterial components as A_1, A_2, B_1, B_2, B_3 and B_4, will be described.

Solvent System for the Distribution of Leucomycin Complex. — The marked difference observed among the solubilities of each of the components of leucomycin complex in aqueous solution at pH 7~8 and in benzene[8], seemed to suggest the use of both solvents for the counter current distribution. Preliminary experiments showed that the addition of methanol to this binary system further improved the resolution. Fig. 1 presents the distribution diagram of leucomycin complex (I), after 150 transfers between the two layers which resulted from a mixture of five parts of benzene, two parts of M/15 sodium phosphate buffer at pH 6.5, and five parts of methanol (Solvent system 1); together with a composite paper chromatogram of leucomycin components in each distribution tube. The results suggested that system 1 could be used for the isolation of A_1, A_2 and B_1.

A solvent system which gave a more minute resolution of leucomycin complex, could be obtained by using much more acid citrate buffer and by adding a sufficient amount of choroform to the triple-system composed of benzene, citrate buffer and methanol. Differing from solvent system 1, the quartet-system separated into two layers very rapidly, though the volume-ratio of these two layers differed to some extent by a slight change of temperature. Fig. 2 illustrates the distribution diagram

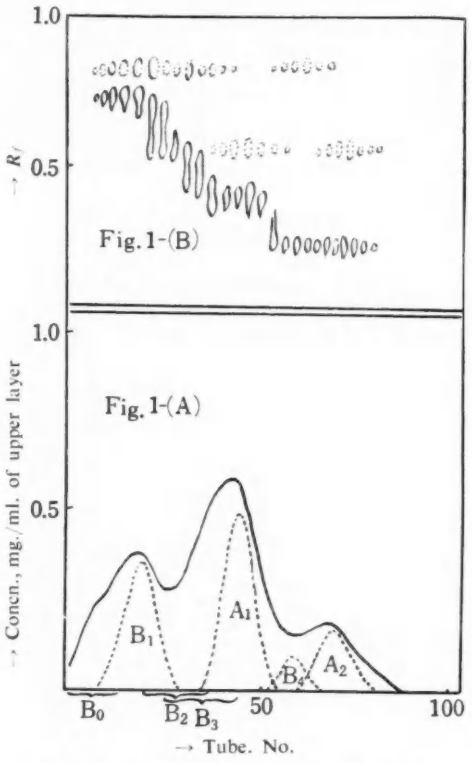

Fig. 1—(A). ---- Counter current distribution of luecomycin complex (I) using "Solvent system 1".

Fig. 1—(B). ---- Composite paper chromatogram of luecomycin components in each distribution tube. ○ developed with *n*-butyl acetate containing phosphate buffer (pH 6). ○ developed with phosphate buffer (pH 8) containing *n*-butyl acetate.

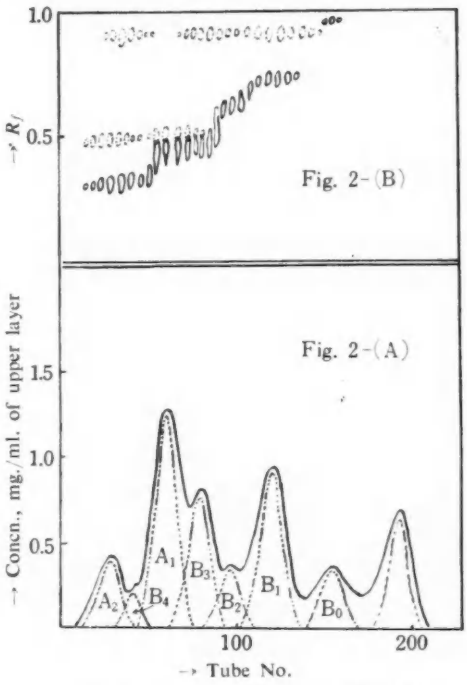

Fig. 2—(A). ---- Counter current distribution of leucomycin complex (I) using "Solvent system 2".

Fig. 2—(B). ----] Composite paper chromatogram of leucomycin components in each distribution tube; ○ developed with *n*-butyl acetate containing phosphate buffer (pH 8) containing *n*-butyl acetate.

13) Y. Sano, T. Hoshi and T. Hata, *J. Antibiotics*, Ser. A7, (3) 88 (1954).

of leucomycin complex (I), after 210 transfers between the two layers which resulted from a mixture of ten parts of benzene, nine parts of M/15 sodium citrate buffer of pH 4.9, eight parts of chloroform and twenty parts of methanol (Solvent system 2); together with a composite paper chromatogram of leucomycin components in each distribution tube. From the appropriate tubes after this distribution, five kinds of antibacterial component could be isolated completely free from other components though the yields of B_2 and of B_3 were not so excellent as that of A_1 A_2 or B_1 due to the partial resolution of the former two.

For the resolution of B components, especially of B_2 and B_4 which were only slightly soluble in benzene, another system composed of chloroform and acid buffer seemed to be promising, as B components showed a moderate solubility in both solvents. In this case, too, the resolution was improved by adding an appropriate amount of a third solvent which could be mixed with upper and lower layers at any ratio, and the effect of acetone seemed to be superior to that of methanol in this solvent system. Fig. 3 shows the distribution diagram of antibiotic IV (see Table I) present in the filtrate fraction from leucomycin complex (I) precipitated at pH 7, after 250 transfers between the two layers which resulted from a mixture of one part of chloroform, two parts of M/15 sodium acetate buffer of pH 4.5, and two parts of acetone (Solvent system 3), together with a composite paper chromatogram of leucomycin components in each distribution tube. From the appropriate fractions after this distribution, all B components, B_1, B_2, B_3 and B_4, could be isolated in a good yield, respectively. The results suggested that the counter current distribution with "Solvent system 3" was the most suitable method for the isolation of four B components; if the most part of A_1 which was the main component of leucomycin complex, had been previously removed.

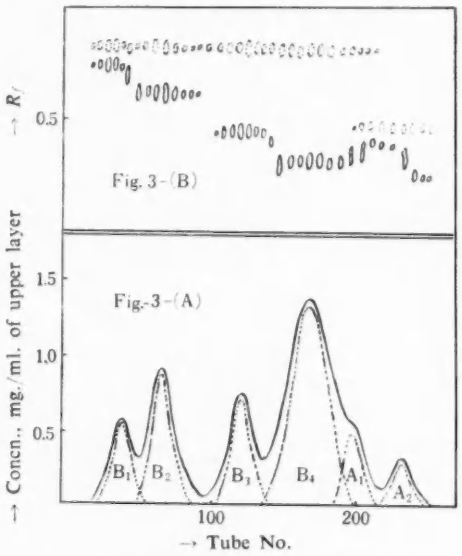

Fig. 3—(A). ---- Counter current distribution of fraction IV (See Table I, B components rich fraction) using "Solvent system 3".

Fig. 3—(B). ---- Composite paper chromatogram in each distribution tube; ○ developed with *n*-butyl acetate containing phosphate buffer (pH 6). ○ developed with phosphate buffer (pH 8) containing *n*-butyl acetate.

Leucomycin A_1 and A_2.—As shown in Fig. 2, the observed distribution curves of A_1 and of A_2, showed no serious disagreement with the theoretical ones calculated from the maximum peak position[14], nor with the distribution of A_1 and A_2 estimated by paper chromatography. The facts seemed to indicate the homogeneity of both the components resolved by counter current distribution. The presumption was verified by the identity of the observed and the calculated re-distribution

TABLE II. PROPERTIES OF LEUCOMYCIN A_1 AND A_2

	A_1	A_2
Partition coefficient K		
Solvent system 1	0.92	2.33
Solvent system 2	0.33	0.14
Solvent system 3	1.86	3.00
$\lambda_{max}^{N/1000\ HCl}(\varepsilon_{max})$	233 mμ (2.45×10^4)	231 mμ (1.98×10^4)
pK'_a	7.1	7.1
Equivalent as base		
Found.	920~950	1220~1250
(Calcd.)	(918)[a]	(1265)[b]
C%; Found. (Calcd.)	60.99 (60.13)	62.13 (61.66)
H%; Found. (Calcd.)	8.72 (8.75)	8.61 (8.70)
N%; Found. (Calcd.)	1.52 (1.54)	1.10 (1.11)
Antibacterial activity (unit/mg.)	1000	910
Content (%) in I	33	19
II	—	—
III	8	4
IV	3	1

a) as $C_{46}H_{81}NO_{17}$
b) as $C_{65}H_{111}NO_{22}$

14) L. C. Craig and O. Cost, *Anal. Chem.*, **21**, 508 (1949).

curves (using "Solvent system 1 or 2" for the samples isolated with "Solvent system 2 or 1", respectively).

In Table II, are summarized the analytical data and some properties of leucomycin A_1 and A_2. There have been reported several macrolides, from picromycin ($C_{25}H_{43}NO_7$)[15] up to magnamycin ($C_{42}H_{67}NO_{16}$)[16]. Minor components A_2 ($C_{65}H_{111}NO_{22}$) seemed to be a macrolide of highest molecular weight, as far as we know. Main component A_1 ($C_{46}H_{81}NO_{17}$), on the other hand, was similar to magnamycin in the molecular weight and pK'_a, though the former had an antibacterial activity higher than that of the latter. In Table II, are also presented the contents of A_1 and A_2, in leucomycin complex and in several fractions derived during the preparation of fraction I. These values calculated from the distribution diagram with "Solvent system 2" were not inconsistent with the A_1- and A_2-content estimated from the elution diagram from a column of Amberlite IRC-50 with a mixture of ethanol and M/15 sodium citrate buffer at pH 5[8]. The results also indicated that both the components were less soluble in aqueous solution at pH 7, less absorbed on a column of active carbon, and more soluble in benzene than B components. Fig. 4 represents infrared spectra of A_1. The presence of OH, C=O (ester) and C=C was presumed from the characteristic absorption at 3450 cm^{-1}, 1750 cm^{-1} and 1680 cm^{-1}, respectively. A shoulder at 1710 cm^{-1} seemed to be due to the presence of the second C=O (lactone).

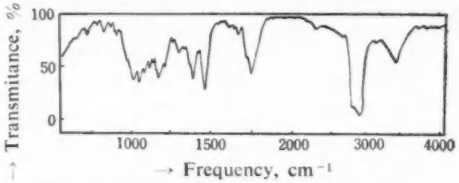

Fig. 4. Infrared spectrum of leucomycin A_1. (in Nujol)

Infrared spectrum of A_2 was extremely close to that of A_1.

Leucomycin B_1, B_2, B_3 and B_4. — Four components, B_1, B_2, B_3 and B_4, found in leucomycin complex as minor components, could be isolated by counter current distribution using "Solvent system 3" from the filtrates III and IV of leucomycin complex(I)precipitated at pH 7[8], from the mother liquid of the recrystallization of leucomycin complex (I); and from the methanol-eluate II of the carbon-column previously treated with *n*-butyl acetate solution of leucomycin[7,8]. As shown in Fig. 3, the distribution curves of these components agreed with the corresponding theoretical curve. The homogeneity of the component so isolated was further verified by analytical chromatography on a column of Amberlite IRC-50[8].

Leucomycin B components (C_{34}—C_{38}) had a molecular weight similar to that of erythromycin A[18], but the pK'_a value (6.8) was similar to those of leucomycin A and magnamycin. The antibacterial activity was considerably lower than that of A_1. In Table III,

TABLE III. YIELDS, PROPERTIES AND ANTIBACTERIAL ACTIVITY OF LEUCOMYCIN COMPONENTS

Component	*K* Solvent system 1	2	3	m. p. °C	C % Found (Calcd.)	H % Found (Calcd.)	N % Found (Calcd.)
B_0	0.1	2.3	—	—	—	—	—
B_1	0.19	1.3	0.15	214.5~216.5	60.30(60.00)	8.22(8.20)	1.99(2.00)[a]
B_2	0.37	0.91	0.28	214.0~216.0	56.85(56.50)	8.14(8.05)	1.66(1.63)[b]
B_3	0.54	0.50	0.67	216.0~217.0	59.39(59.73)	7.65(7.72)	2.05(2.05)[c]
B_4	1.50	0.19	1.22	221.0~223.8	56.27(56.81)	7.59(7.64)	1.81(1.78)[d]

Component	Antibacterial activity (unit/mg.)*	$\lambda_{max}^{N/1000\ HCl}$ (ε_{max})	Yield (%) from I*	II**	III**	IV***
B_0	<10	—	2	8	0	0
B_1	100	234 mμ(2.24×10^4)	11	23	50	24
B_2	215	234 mμ(2.47×10^4)	6	12	20	29
B_3	570	234 mμ(2.32×10^4)	19	38	27	13
B_4	700	233 mμ(2.45×10^4)	8	20	9	30

* Leucomycin complex (I); 560 unit/mg. ** Using "Solvent system 2".
*** Using "Solvent system 3".
a) as $C_{35}H_{59}NO_{13}$ b) as $C_{38}H_{65}NO_{16}$ c) as $C_{34}H_{53}NO_{13}$ d) as $C_{35}H_{59}NO_{16}$

15) H. Brockmann et al., *Ber*, **84**, 284 (1951).
16) R. L. Wagner, F. A. Hochstein and K. Murai, *J. Am. Chem. Soc.*, **75**, 4684 (1953).
17) E. H. Flynn, M. V. Sigal and F. R. Wiley, ibid., **76**, 3121 (1954).

are summarized the analytical data, some properties and the content in leucomycin complex (I) and in several fractions II, III and IV. The last data indicated that B components could be fractionated, and that the fractions thus obtained could be further separated into two groups, B_1 and B_3 rich III, and B_2 and B_4 rich group IV. It seems to be interesting that the original strain of *Streptomyces kitasatoensis* produced as many as six kinds of macrolide, while the mutant (strain No. L-149-373) gave only A_1 and A_2 without any decrease of the weight of total antibiotics. The elucidation and comparison of the structure of these components might give valuable information on the biosynthesis of macrolides.

Experimental

Materials.—Leucomycin complex (I) and the fractionated antibiotics II, III, IV were prepared by the methods summarized in Table I.

Counter Current Distribution.—The procedure was achieved at 15~20°C in an automatic "Craig-type" apparatus having 300 transfer tubes No. 555 F, Mitamura Shoten, Tokyo). The sample (1~10 g.) was added as a concentrated solution in the lower solvent layer (5~10%) into the first few tubes. The volume of the upper and the lower layer in each distribution tube was 10 cc. each. The partition coefficient of distributed components was calculated from the peak position on the distribution diagram and the total transfer-number. The theoretical distribution curve was calculated from the partition coefficient so obtained, according to Craig's method[4].

Determination of the Concentration of Leucomycin.—The concentration was assayed by the photometry of red brown color which was produced by mixing 0.5 cc. of the sample (aqueous layer in the distribution tube) with 2.0 cc. of concentrated sulfuric acid[5]. The concentration in organic-solvent rich layer, was calculated from the above-mentioned concentration in aqueous layer and the calculated partition coefficient.

Paper Chromatography of Leucomycin Components.—Paper chromatography of leucomycin in each distribution tube was achieved by the method already reported[7], using 0.02 cc. of the organic-solvent rich phase as the sample.

Crystallization of Each Component.—The leucomycin components separated by counter current distribution, was crystallized from the aqueous solution by adjusting the pH to 8 according to the method reported already[3].

Antibacterial Activity.—The assay of the antibacterial activity of the components so purified, was done by the Bio-assay Division, Toyo Jozo Co. Ltd., according to the usual cup assay method with the use of *Baccillus subtilis* No. 209 as the test organism.

Absorption Specta.—Absorption spectra were measured by Hitachi Spectrophotometer Model DUP-2.

pK'_a.—pK'_a was measured on the sample solution in a dimethylformamide (60%) at a concentration of 0.05 per cent, by titrating with 1 N hydrochloric acid with the use of Toa-denpa pH meter HM-5.

We are greatly indebted to Mr. S. Suda for his assistance in paper chromatographic analysis of the distributed fractions.

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Studies on Seven-Membered Heterocyclic Compounds Containing Nitrogen. IV. Hexahydro-1, 2, 5-Triazazulene

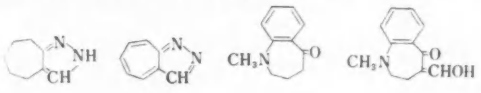
By Shiro MOROSAWA

(Received February 6, 1960)

It has been found that hexahydro-1, 2-diazazulene (I)[1-3] was prepared from 2-hydroxymethylenecycloheptanone. Buchta[4] has made only a simple statement that W. Treibs succeeded in dehydrogenation of the hydroazazulene by chloranil to yield 1, 2-diazazulene (II), but no further detailed report was given. The present author has synthesized hitherto unknown hexahydro-1, 2, 5 (or 1, 2, 6)-triazazulene (XIa or XIb), having one nitrogen atom in the seven-membered ring in satisfying yield. Spectral studies have shown that the former

1) O. Wallach, *Ann.*, **329**, 109 (1903).
2) W. Treibs and H. J. Neupert, ibid., **595**, 219 (1955).
3) E. Buchta and J. Kranz, ibid., **601**, 170 (1956).
4) E. Buchta et al., *Angew. Chem.*, **67**, 77 (1955).

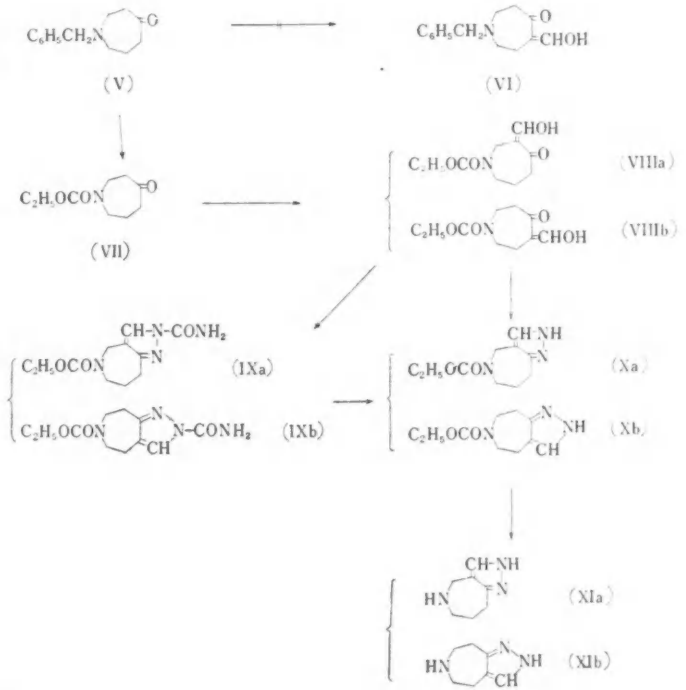
structure is more reasonable. A preliminary test of dehydrogenation was quite unsuccessful, but further attempts are in progress.



(I) (II) (III) (IV)

N-Methyl type azasuberenone, 1-methyl-2, 3, 4, 5-tetrahydro-5-keto-1-benzazepine (III)[5] has been reported to afford 4-hydroxymethylene derivative (IV) in 72% yield by the reaction with ethyl formate in the presence of sodium methoxide in benzene. Under the same condition, however, *N*-benzyl type azasuberone, 1-benzyl-1-azacycloheptan-4-one (V)[6] gave only a trace of hydroxymethylene compound, which certified as bis-2, 4-dinitrophenylhydrazone, leaving much residue on distillation. 1-Ethoxycarbonyl-1-azacycloheptan-4-one (VII) derived from V was subjected to the similar treatment and 1-ethoxycarbonyl-3 (or 5)-hydroxymethylene-1-azacycloheptan-4-one (VIIIa or VIIIb)*, b. p. 127～130°C/0.7 mmHg was obtained in 72.5% yield as a colorless oil. Reaction of hydrazine hydrate with VIII in ether gave a stable pyrazole derivative (Xa or Xb), b. p. 183～185°C/0.3 mmHg in 87.6% yield. X was also derived from VIII cyclic semicarbazone (IXa or IXb), m. p. 159～159.5°C by hydrolysis. X afforded a picrate of m. p. 136.5～137.5°C and a chloroplatinate of m. p. 184°C (decomp.) respectively. Deethoxycarbonylation of X by hydrogen bromide in glacial acetic acid gave hydrobromide of XIa or XIb in 84% yield as hygroscopic colorless long prisms which softened at above 260°C. Free base, XIa or XIb, was liberated almost quantitatively from the hydrobromide with alkali as hygroscopic, colorless hexagonal prisms of m. p. 155.5～156.5°C. XI formed a picrate of m. p. 220～221°C (decomp.), which was unstable to light and turned brown on standing.

As a preliminary examination of dehydrogenation 4, 5-cyclohepteno-7-methylthiazole (XIV), b. p. 109～111°C/15 mmHg which was prepared from cycloheptanone** (XII) by NBS bromination and condensation with thioacetamide was subjected to the dehydrogenation

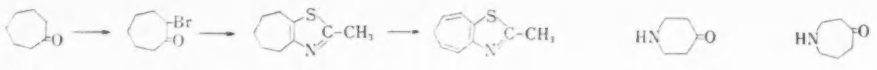


5) B. D. Astill and V. Beokelheide, *J. Am. Chem. Soc.*, **77**, 4079 (1955).

6) (a) A. Yokoo and S. Morosawa, This Bulletin, **29**, 631 (1956); (b) S. Morosawa, ibid., **31**, 418 (1958).

* Degradative studies will be reported later.

** The author wishes to thank Professor Tetsuo Nozoe (Tohoku University) for donating the sample.



(XII) (XIII) (XIV) (XV) (XVI) (XVII)

with 10% palladium on carbon at elevated temperature. Thus 4, 5-cycloheptatrieno-7-methylthiazole (XV) was obtained as a colorless oil, b. p. 104°C/12 mmHg, XV gave a picrate of m. p. 147~148°C. XI, however, was decomposed under the same condition with evolution of hydrogen. Ultraviolet absorption spectra of XI, XIV and XV are given in Fig. 1, together with that of the condensation product of XIV ethiodide with *p*-dimethylaminobenzaldehyde.

It appeared of interest to obtain a unique product in the formation of the hydroxymethylene compound (VIII) from the asymmetrical ring ketone (VII). The structure of the pyrazole derivative (XI) was estimated by the following spectral studies. It has already been recognized[7] that the band arising from the hydrogen bending vibrations of methylene appeared near the 1450 cm^{-1} region and shifted in some degree higher when attached to the nitrogen atom and somewhat lower to carbon-carbon or carbon-oxygen double bond. As shown in Fig. 2, 1-azacyclohexane-4-one (XVI)[8],* gave rise to only two bands near the region at 1469 and 1428 cm^{-1}, presumably arising from 2 (or 6)- and 3 (or 5)-methylene of the ring respectively. 1-Azacycloheptan-4-one (XVII)**, on the other hand, indicated at least three bands at 1464, 1452 and 1431 cm^{-1}, probably due to 2 (or 7)-, 6- and 3 (or 5)-methylene respectively. Hydrochlorides of XVI and XVII also gave rise to two and three bands respectively, corresponding to the above absorption bands. XV was expected to show two bands near the region arising from methyl*** at 2-position of the thiazole ring and methylene in the seven-membered ring, and in fact two bands at 1457 and 1437 cm^{-1} were observed. From a consideration of these facts it became clear that the methylenes in the nitrogen containing ring ketone were distinguishable from each other in the infrared

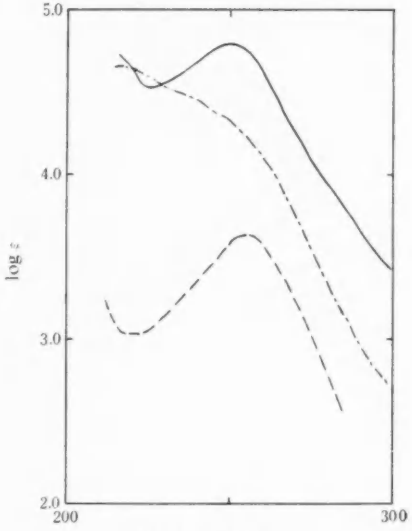


Fig. 1. (in methanol)

—— XI, ——— XIV, ———— XV

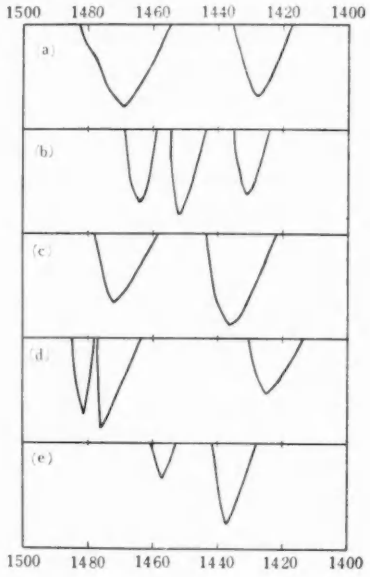


Fig. 2.

(a) XVI; (b) XVII; (c) XVI hydrochloride; (d) XVII hydrochloride; (e) XV

7) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules", Methuen & Co. Ltd., London (1958), p. 20.
8) E. Königs and L. Neumann, *Ber.*, **48**, 956 (1915).

* Prepared from 1-benzyl-1-azacyclohexan-4-one[6b] by catalytic reduction in the presence of palladous oxide, b. p. 56~57°C/6 mmHg. It began to polymerize into a white solid within an hour after distillation.

** Liberated by potassium carbonate from its hydrochloride[6a], b. p. 95~96°C/15 mmHg.

*** According to Bellamy[7], the band arising from the methyl group adjacent to the carbon atom appeared near 1450 cm^{-1} in relatively low intensity.

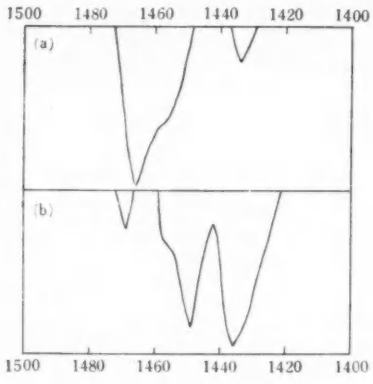


Fig. 3.
(a) XI; (b) XI hydrobromide

absorption spectra. The pyrazole derivative (XI) indicated, as seen in Fig. 3, three bands at 1466, 1458 (shoulder) and 1434 cm^{-1}. It may be assumed that the former band is due to 6-methylene and the latter to 8, the shoulder being due to overlapping of bands arising from 4- and 7-methylene. Hydrobromide of XI distinctly showed three principal bands at 1469, 1449 and 1436 cm^{-1} together with a shoulder at 1456 cm^{-1} which probably arose from 4-methylene. From these spectral data it may be concluded that XI has an angular form (XIa) rather than a linear one (XIb) and therefore the hydroxymethylene compound is in the form of VIIIa.

Experimental

1-Ethoxycarbony-1-azacycloheptan-4-one (VII).—A solution of 15 g. of V hydrochloride[6a,b] in 200 cc. of water was shaken with hydrogen in the presence of 0.2 g. of palladous oxide under normal temperature and pressure. After the theoretical amount of hydrogen was consumed the catalyst was filtered off and evaporated to a smaller volume under reduced pressure. To this were added a solution of 2.7 g. of sodium hydroxide in 5 cc. of water and 14.7 g. of anhydrous potassium carbonate. The mixture was kept at 10°C and 15 g. of ethyl chlorocarbonate was added dropwise during 45 minutes with stirring, followed by further stirring for 1 hour at the same temperature. Precipitates were collected and washed well with ether, and the filtrate was thoroughly extracted with ether. The water layer was evaporated under reduced pressure until precipitation began and treated as before. The ethereal solutions were combined and dried over anhydrous potassium carbonate. Evaporation of ether and vacuum distillation gave 11.5 g. (99.1%) of a colorless oil, b. p. 117°C/1 mmHg The oil was fairly soluble in water and did not give a bisulfite addition compound.

Found: N, 7.66. Calcd. for $C_9H_{15}O_3N$: N, 7.56%.

1-Ethoxycarbonyl-3(or 5)-hydroxymethylene-1-azacycloheptan-4-one (VIIIa or VIIIb).—A solution of 6 g. of VII and 9.5 g. of ethyl formate in 50 cc. of dry benzene was added with swirling to an ice cold suspension of crushed methanol-free sodium methoxide[9] (from 1.6 g. of sodium) in 50 cc. of dry benzene, and the whole was evacuated and filled with nitrogen. After the mixture had been allowed to stand at room temperature for 3 hours, it was boiled under gentle reflux for 1 hour. After cooling, 10 cc. of water was added and the aqueous layer was separated. The benzene solution was washed twice with 10% sodium hydroxide solution. The combined water layer was washed with ether and adjusted to pH 3.4 by adding hydrochloric acid. A reddish orange oil deposited was extracted three times with benzene. The acidic water layer was evaporated to a smaller volume under reduced pressure and nitrogen atmosphere and extracted with benzene. The benzene extracts were united, washed three times with small portions of saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Evaporation of benzene and vacuum distillation of the residue under nitrogen gave 5 g. of a colorless oil, b.p. 127~130°C/0.7 mmHg in 72.5% yield. It gave a deep purple coloration with ferric chloride solution.

Found: N, 6.80. Calcd. for $C_{10}H_{15}O_4N$: N, 67.5%.

2, 4-Dinitrophenylhydrazone, orange prisms, m.p. 172°C (from methanol).

Found: N, 19.24. Calcd. for $C_{15}H_{19}O_6N_5$: N, 19.17%.

VIII Cyclic Semicarbazone (IXa or IXb).—A solution of 2.2 g. of VIII in 9 cc. of glacial acetic acid was added to a separately prepared solution of 1.7 g. of semicarbazide hydrochloride and 1.7 g. of anhydrous sodium acetate in as small an amount of water as possible. After the mixture was allowed to stand for a few days with 1 cc. of concentrated sulfuric acid, 50 cc. of water was added to deposit gradually 1.0 g. of cyclic semicarbazone in colorless needles, m. p. 155°C. Recrystallization from ethanol raised the m. p. to 159~159.5°C.

Found: N, 22.16. Calcd. for $C_{11}H_{16}O_3N_4$: N, 22.21%.

5(or 6)-Ethoxycarbonyl-1, 2, 5(or 1, 2, 6)-triazazulene (Xa or Xb).—(a) To a solution of 5 g. of VIII in 50 cc. of ether was added dropwise under stirring and ice-water cooling 1.2 g. of hydrazine hydrate (100%), followed by an additional stirring for 1 hour. After decantation of the ethereal solution, a large excess of anhydrous potassium carbonate was added to the viscous water layer in order to remove the water completely. Ether was added, agitated well and decanted repeatedly. The combined ethereal solution was dried over anhydrous potassium carbonate and the ether was removed by distillation. Vacuum distillation of the residue gave 4.3 g. of a colorless viscous oil, b. p. 183~185°C/0.3 mmHg in 87.6% yield.

9) W. S. Johnson and H. Posvic, *J. Am. Chem. Soc.*, **69**, 1361 (1947).

Found: N, 20.15. Calcd. for $C_{10}H_{15}N_2O_4$: N, 20.08%.

A **picrate** derived from the above oil showed, after several recrystallizations from ethanol, m. p. 136.5~137.5°C with sintering at about 80°C.

Found: N, 17.53. Calcd. for $C_{10}H_{15}O_2N_3 \cdot C_6H_3O_7N_3 \cdot C_2H_6O$: N, 17.35%.

After drying at 100°C for 1 hour the nitrogen content varied to 19.38%. (Calcd. for $C_{10}H_{15}O_2N_3 \cdot C_6H_3O_7N_3$: N, 19.17%).

The oil also afforded a cream yellow **chloroplatinate,** m. p. 184°C (decomp.) (from aqueous ethanol containing 1 drop of concentrated hydrochloric acid).

Found: N, 10.50. Calcd. for $(C_{10}H_{15}O_2N_3)_2 \cdot H_2PtCl_6$: N, 10.14%.

(b) A mixture of 1.35 g. of IX, 1.7 cc. of concentrated sulfuric acid and 5.1 cc. of water was heated under reflux for 15 minutes. After cooling it was made alkaline by adding aqueous ammonia, extracted with benzene and dried over anhydrous potassium carbonate. Benzene was removed and the residue was distilled in vacuo to give 1.0 g. of colorless viscous oil, b.p. 201°C/0.7 mmHg in 89.3% yield. (Found: N, 19.79%). The **picrate** formed was not depressed on admixture with that described above, m. p. and mixed m. p. 137°C. (Found: N, 17.61%).

Hexahydro-1, 2, 5 (or 1, 2, 6)-triazazulene (XIa or XIb).—A solution of 1.5 g. of X in 15 cc. of glacial acetic acid was saturated with dry hydrogen bromide under ice-water cooling. After standing overnight at room temperature, the solution was heated slowly to 90°C and kept for 2 hours at the same temperature, followed by refluxing for 1 hour. The hydrobromide deposited during the refluxing was separated by decantation, washed twice with a small amount of ethanol and recrystallized from methanol and ether to yield 1.4 g. of hygroscopic, colorless long prisms, which softened at above 260°C, and the second crop of the crystal, 0.4 g. was obtained from the filtrate. The total yield was 84%.

Found: N, 13.83. Calcd. for $C_7H_{11}N_3 \cdot 2HBr$: N, 14.05%.

To a solution of 7.5 g. of the hydrobromide in a small amount of water anhydrous potassium carbonate was added to make it sufficiently alkaline and the mixture was evaporated to dryness under reduced pressure. The residual mass was dried in a desiccator and extracted in the Soxhlet apparatus with isopropyl ether for 15 hours to give 3.4 g. of somewhat hygroscopic, hexagonal **free-base,** m. p. 155.5~156.5°C in 99% yield. An analytical specimen was recrystallized from benzene and ethanol.

Found: C, 61.40; H, 8.22; N, 30.75. Calcd. for $C_7H_{11}N_3$: C, 61.29; H, 8.08; N, 30.63%.

The free base and a saturated ethanolic solution of picric acid formed a picrate, which was recrystallized from ethanol to yellow rhombo prisms, m. p. 220~221°C (decomp.). These gradually turned brown on standing.

Found: N, 23.04. Calcd. for $C_7H_{11}N_3 \cdot C_6H_3O_7N_3$: N, 22.94%.

NBS Bromination of Cycloheptanone.—A mixture of 12.4 g. of cycloheptanone (b. p. 174~181°C), 25 g. of NBS and 1.5 g. of benzoyl peroxide in 600 cc. of carbon tetrachloride was boiled under reflux for 5 hours on a water bath. Initially the mixture was gradually colored, and reaction suddenly started to make it colorless with the evolution of much hydrogen bromide. After cooling in ice-water succinimide was separated, and the filtrate was washed with 50 cc. of 40% potassium carbonate solution and with 10 cc. of water and finally dried over anhydrous potassium carbonate. The solvent was removed and the residue was distilled in vacuo to yield 11 g. of 2-bromocycloheptanone (XIII) as a colorless oil, b. p. 90~130°C/5 mmHg. This was fractionated into three parts, b. p. 90~101°C/5 mmHg, 101~111°C/5 mmHg and 111~128°C/5 mmHg. These, however, gave the same thiazole derivative as described below.

Condensation of XIII with Thioacetamide.—A solution of 11 g. of XIII and 6 g. of thioacetamide in 20 cc. of ethanol was refluxed on a water bath for 5 hours. After removing ethanol and heating the residue for 5 hours in an oil bath kept at 160°C, 40 cc. of 4N hydrochloric acid was added and extracted three times with each 20 cc. portion of ether. The combined ethereal solution was washed with 10 cc. of 4N hydrochloric acid. Acidic solutions were united, made alkaline by adding anhydrous potassium carbonate and 5 cc. of 5N sodium hydroxide solution, and extracted three times with each 20 cc. portion of ether. After drying over anhydrous potassium carbonate, the ether was expelled and the residue was distilled in vacuo to yield 1.4 g. of **4, 5-cyclohepteno-2-methylthiazole (XIV)** as a colorless oil, b. p. 109~111°C/15 mmHg.

Found: N, 8.06. Calcd. for $C_9H_{13}NS$: N, 8.38%.

Ethanolic solution of XIV was boiled with an excessive picric acid to form a **picrate,** which was recrystallized three times from ethanol to yellow crystals, m. p. 129~131°C.

Found: N, 13.84. Calcd. for $C_9H_{11}NS \cdot C_6H_3O_7N_3$: N, 14.15%.

Ethiodide of XIV was obtained as an oily substance by refluxing an ethanolic solution of 0.2 g. of XIV with an excessive ethyl iodide for 8 hours, followed by the addition of ether. This, however, gave a crystalline condensation product assumed to be **4, 5-cyclohepteno-2-(*p*-dimethylaminostyryl)-3-ethylthiazolium iodide** by refluxing with *p*-dimethylaminobenzaldehyde for 8 hours in the presence of a small amount of piperidine and adding ether. The condensation product was recrystallized from ethanol to afford 50 mg. of red crystals, m. p. 219~220°C (decomp.).

Found: N, 5.88. Calcd. for $C_{20}H_{27}N_2SI$: N, 6.17%.

The red crystals showed absorption maximum at 480 mμ.

Dehydrogenation of XIV.—In a 25 cc. hard ground glass flask jointed with an air condenser, the top of which was connected to a measuring bottle, were placed 1.5 g. of XIV, 1.5 g. of 10% palladium on carbon and 1 g. of roughly crushed boiling stone, and heated in an electric oven. Hydrogen began to evolve when the temperature of the oven indicated about 390°C. About 450 cc. of hydrogen had been collected

after heating for 6 hours at 440~460°C. The reaction mixture was first washed out with hot benzene and then with ether. After drying the combined organic solution over anhydrous magnesium sulfate, the solvent was removed and the residue was distilled in vacuo to yield 0.7 g. of **4, 5-cycloheptatrieno-2-methylthiazole** (**XV**) as a colorless liquid, b. p. 104°C/12 mmHg.

Found: C, 65.95; H, 5.66; N, 8.70. Calcd. for C_9H_9NS: C, 66. 24; H. 5.56; N, 8.58%.

A **picrate** derived from the liquid was recrystallized three times from ethanol in yellow crystals, m. p. 147~148°C.

Found: N, 14.50. Calcd. for $C_9H_9NS \cdot C_6H_3O_7N_3$: N, 14.27%.

The author wishes to thank Professor A. Yokoo (this laboratory) for his frequent helpful advice and Mr. K. Kurosaki (Research Laboratory of Fuji Photo Film Company) for the infrared measurements and valuable suggestions. Thanks are also due to Mr. A. Kondo (the Department of Organic Chemistry, Tokyo Institute of Technology) for carrying out the carbon and hydrogen micro-analyses.

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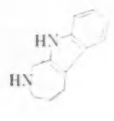
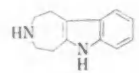
Studies on Seven-Membered Heterocyclic Compounds Containing Nitrogen. V. 2, 3, 4, 5-Tetrahydro-1(H)-indolo[2, 3-c]azepine

By Shiro MOROSAWA

(Received February 6, 1960)

The initial purpose of the present investigation was to prepare 2, 3, 4, 5-tetrahydro-1(H)-indolo[2, 3-c]azepine (Ia) or 1, 2, 4, 5-tetrahydro-3(H)-indolo[3, 2-d]azepine (Ib) which suggests a possibility of dehydrogenation into 2, 3-benzo-1, 7-diazazulene (IIa) or 2, 3-benzo-1, 6-diazazulene (IIb). As similar compounds of this type, 4-ethyl-5, 6, 7, 12-tetrahydro-2-methylindolo[3,2-d][1]-benzazepine (III)[1], 6,7-dihydro-1-methyl-2, 3-benzindolo[2' : 3'-4 : 5]-azepine (IV)[2] and 1, 2, 3, 4, 5, 10-hexahydro-7-hydroxy-3-methylazep[4, 5-b]indole (V)[3] have been known. These are, however, compounds of *N*-alkyl or condensed type of phenyl and seven-membered ring, and it may be impossible to bring them into an azulene system by dehydrogenation. After several attempts the author synthesized 2-ethoxycarbonyl-2, 3, 4, 5-tetrahydro-1(H)-indolo[2, 3-c]azepine (XXII), 2-ethoxycarbonyl-7-methoxy-2, 3, 4, 5-tetrahydro-1(H)-indolo[2, 3-c]azepine (XXIII) (as picrate only) and Ia (as picrate only), each of which was assumed to have an angular structure as written from spectral data.


(Ia)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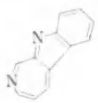
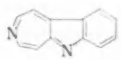

(IIa)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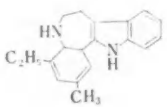
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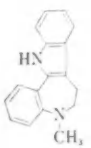
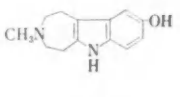
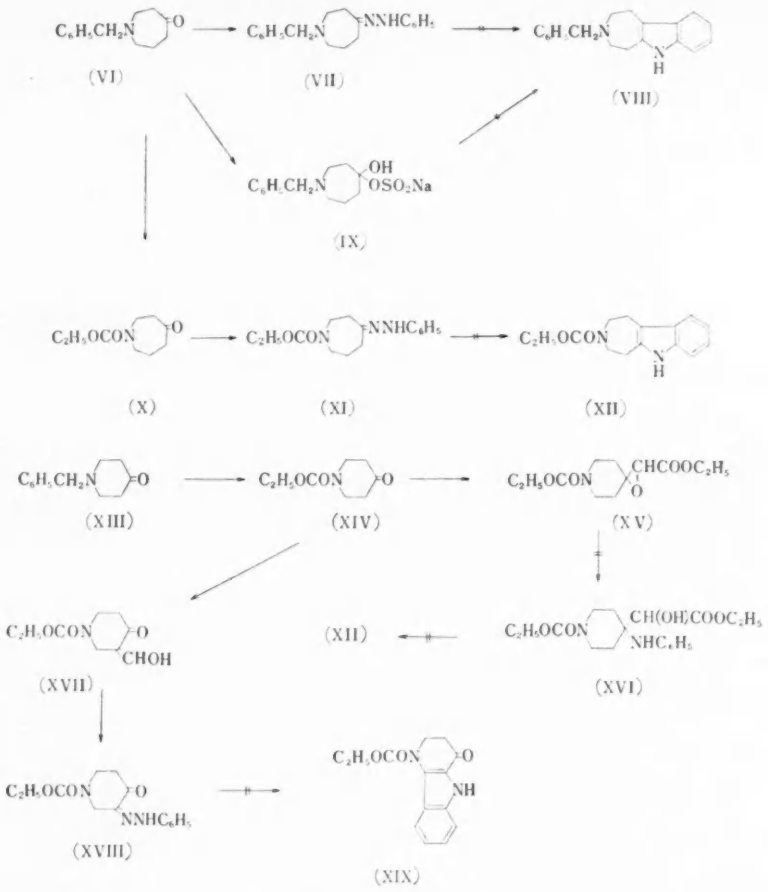

(IV)


(V)

1) H. B. MacPhillamy et al., *J. Am. Chem. Soc.*, **80**, 2172 (1958).

2) J. T. Braunholtz and F. G. Mann, *J. Chem. Soc.*, 1958, 3377.

3) J. Harley-Mason and A. H. Jackson, ibid., 1955, 374.



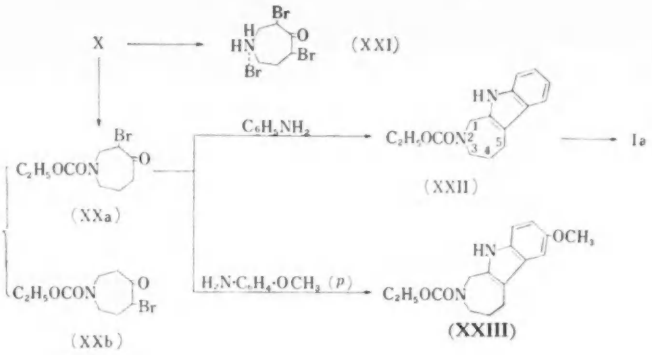
First of all the author attempted cyclization of phenylhydrazone (VII) and of its hydrochloride of 1-benzyl-1-azacycloheptan-4-one (VI)[4] under the condition of Fischer indole synthesis and under other similar conditions. They have shown a considerable resistance in the cyclizations and were recovered unchanged. In some cases, only a slight indole-like odor and a positive pine-splinter test were observed. Phenylhydrazone (XI) of 1-ethoxycarbonyl-1-azacycloheptan-4-one (X)[5] was also not cyclized with hydrogen chloride in ethanol. An application of the carbazole synthesis to bisulfite compound (IX)[6] of VI resulted in the recovery of VII.

Martynov's method[7], which has obtained 2, 3-pentamethyleneindole in good yield from cyclohexanone via glycidic acid derivative, was applied to 1-ethoxycarbonyl-1-azacyclohexan-4-one (XIV), but the addition reaction of glycidic acid derivative (XV) with aniline failed.

Mühlstädt and Treibs[8] have synthesized 1-keto-2, 3, 4, 5-tetrahydroheptiadole from monophenylhydrazone of cycloheptane-1, 2-dione, and Kent[9] has also obtained 1-keto-1, 2, 3, 4-tetrahydrocarbazole from cyclohexane-1, 2-dione monophenylhydrazone. As a preliminary experiment 1-ethoxycarbonyl-1-azacyclohexane-3, 4-dione monophenylhydrazone (XVIII) derived from XIV was treated under the above conditions, but no expected compound was obtained.

Campbell and McCall[10] have obtained some tetrahydrocarbazoles by heating 2-chlorocyclohexanone with arylamines. In a similar manner, a bromoketone (XXa or XXb)*, which

4) S. Morosawa, This Bulletin, **31**, 418 (1958).
5) S. Morosawa, ibid., **33**, 1108 (1960).
6) S. Morosawa, ibid., **33**, 575 (1960).
7) V. F. Martynov, *Chem. Abstr.*, **49**, 3124 (1955).
8) M. Mühlstädt and W. Treibs, *Ann.*, **608**, 38 (1957).
9) A. Kent, *J. Chem. Soc.*, **1935**, 976.
10) N. Campbell and E. B. McCall, ibid., **1950**, 2870.
* Situation of bromine atom is now under investigation by degradative method.



derived from X by NBS bromination, with aniline and *p*-anisidine gave rise to the desired compounds, XXII and XXIII (as picrate) respectively. The elimination of ethoxycarbonyl groupe of XXII gave Ia as a picrate. According to the same procedure of the formation of 3, 5, 7-tribromotropone[11], X was brominated in glacial acetic acid with bromine. But it resulted in elimination of the ethoxycarbonyl group, yielding 3, 5-dibromo-1-azacycloheptan-4-one hydrobromide (XXI). Ultraviolet absorption spectrum of XXII is given in Fig. 1, being compared with that of indole.

In the NBS oromination of X two kinds of bromide, 3-bromo (XXa) and 5-bromo (XXb) derivatives were expected. But only one kind of bromide was obtained. Sprague[12] has reported that NBS bromination of tetrahydro-1, 3-thiapyrone yielded 2-bromo compound exclusively. Similarly one might assume in the 1-azacycloheptan-4-one ring that activated 3-position by neighboring carbonyl, though weak, would be further affected more by the inductive effect of the nitrogen atom than 5-position, making the bromine attack on the position to give 3-bromo compound. Consequently XXII and XXIII may be assumed to be angular structures as shown. This accorded with the spectral data as follows:

The picrate of I indicated four bands near the region due to the hydrogen bending vibration of methylene at 1495, 1486, 1466 and 1430 cm^{-1}. The band at 1495 cm^{-1} was due to stretching vibration of the double bond in benzene ring and the other three to 3-, 1-(overlapping with 4-) and 5-methylene in the seven-membered ring as mentioned in the foregoing paper[5]. XXII, on the other hand, gave a broad absorption band in the region owing to overlapping of the above three bands with that arising

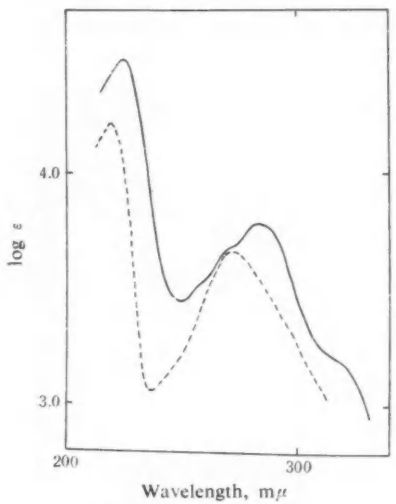


Fig. 1. (in methanol).
—— XXII; ---- indole.

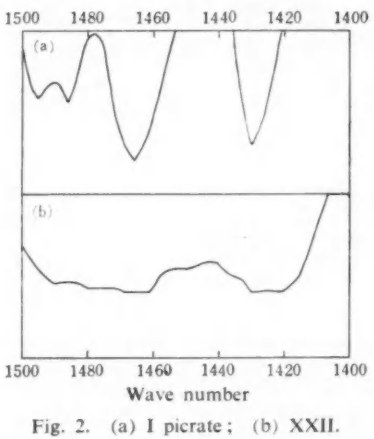


Fig. 2. (a) I picrate; (b) XXII.

11) T. Nozoe, Y. Kitahara, T. Ando and S. Masamune, *Proc. Japan Acad.*, **27**, 415 (1951).
12) R. H. Sprague, *J. Am. Chem. Soc.*, **79**, 2275 (1957).

from methyl and methylene in the ethoxycarbonyl group. Infrared absorption spectra of these two compounds are given in Fig. 2.

Experimental

1-Benzyl-1-azacycloheptan-4-one Phenylhydrazone (VII).—To a solution of 1 g. of recrystallized phenylhydrazine hydrochloride and 1.6 g. of anhydrous sodium acetate in 10 cc. of water was added 0.8 g. of VI. Ethanol was added to the mixture until a clear solution was obtained and heated on a water bath for 30 minutes. Crystals formed on cooling were recrystallized from diluted ethanol to give 1.1 g. (80%) of **VII hydrochloride** in light greenish yellow needles, m. p. 225°C (decomp.).

Found: N, 12.39. Calcd. for $C_{19}H_{23}N_3 \cdot HCl$: N, 12.74%.

The hydrochloride was mixed with an excessive diluted potassium carbonate solution and evaporated to dryness under reduced pressure. The residual mass was treated with benzene, and benzene was expelled to leave **free phenylhydrazone** as an oil which crystallized on standing. It was recrystallized from diluted ethanol in light yellow needles, m. p. 75°C.

Found: N, 14.98. Calcd. for $C_{19}H_{23}N_3$: N, 14.32%.

1-Ethoxycarbonyl-1-azacycloheptan-4-one Phenylhydrazone (XI).—A mixture of 1.6 cc. of phenylhydrazine, 1.6 cc. of glacial acetic acid and 0.8 g. of X was treated as above. Crude product 1.2 g. (100%), m. p. 130°C (decomp.), was recrystallized from diluted ethanol to give 0.9 g. of XI as yellow needles, m. p. 130°C (decomp.).

1-Ethoxycarbonyl-1-azacyclohexan-4-one (XIV).—According to the same procedure as that of the formation of X, 15 g. of 1-benzyl-1-azacyclohexan-4-one (XIII)[4] yielded 12.3 g. (90.8%) of XIV, boiling at 93~94°C/1 mmHg as a colorless oil.

Found: N, 8.12. Calcd. for $C_9H_{15}O_3N$: N, 8.18%.

2,5-Diethoxycarbonyl-1-oxa-5-azaspiro(5,2)octane (XV).—To a mixture of 3.5 g. of XIV and 2.4 g. of ethyl monochloroacetate was added a solution of 0.74 g. of metallic potassium in 25 cc. of tertiary butanol under stirring and ice-water cooling during 30 minutes in the nitrogen atmosphere. After an additional stirring for 1 hour the butanol was expelled under reduced pressure and the residue was dissolved in 15 cc. of water. The solution was adjusted to pH 2.0 with hydrochloric acid and extracted with ether. The ethereal solution was washed once with water and dried over anhydrous sodium sulfate. The ether was removed and the residue was distilled in vacuo to give 2.5 g. (47.7%) of a colorless viscous oil, b.p. 146~150°C/1.5 mmHg.

Found: N, 5.21. Calcd. for $C_{12}H_{19}O_5N$: N, 5.44%.

1-Ethoxycarbonyl-3-hydroxymethylene-1-azacyclohexan-4-one (XVII).—A solution of 12.3 g. of XIV and 10.6 g. of ethyl formate in 150 cc. of dry benzene was added with swirling to an ice cold suspension of crushed methanol-free sodium methoxide[13] (from 3.3 g. of sodium) in 150 cc. of dry benzene. The system was evacuated and filled with nitrogen, and allowed to stand at room temperature overnight. Precipitates were dissolved by adding 60 cc. of water. The benzene layer was separated and washed four times with each 10 cc. of 5% solution of sodium hydroxide. The water layer and the washings were united, washed once with ether and acidified with concentrated hydrochloric acid to deposit an orange oil. The oil was taken up in benzene and the water layer was concentrated under reduced pressure, and extracted further with benzene. Benzene extracts were united, washed five times with a small volume of saturated sodium chloride solution and dried over anhydrous magnesium sulfate. After removal of benzene, the vacuum distillation gave 3.5 g. (24.5%) of a colorless viscous oil, boiling at 130~131°C/2 mmHg.

Found: N, 7.06. Calcd. for $C_9H_{13}O_4N$: N, 7.03%.

The oil gave a **monosemicarbazone**, m. p. 156.5°C (Found: N, 22.09%) and a **cyclic semicarbazone**, m. p. 128.5°C (Found: N, 23.28%).

1-Ethoxycarbonyl-1-azacyclohexan-3,4-dione Monophenylhydrazone (XVIII).—To a mixture of 0.63 g. of redistilled aniline, 0.67 cc. of concentrated sulfuric acid and 5 cc. of water was added dropwise a solution of 0.47 g. of sodium nitrite in 1.8 cc. of water under stirring and ice-water cooling, followed by the addition of a saturated solution of 1.1 g. of anhydrous sodium acetate. Then a solution of 1 g. of XVII in 3 cc. of ether was added dropwise and the resultant mixture was stirred for 15 minutes while cold and for 30 minutes at room temperature. The orange crystals which separated were collected and recrystallized five times from methanol to give 0.6 g. (43.5%) of XVIII, m. p. 116~117°C.

Found: N, 15.07. Calcd. for $C_{14}H_{17}O_3N_3$: N, 15.26%.

3(or 5)-Bromo-1-ethoxycarbonyl-1-azacycloheptan-4-one (XXa or XXb).—A mixture of 7.4 g. of X, 0.3 g. of benozyl peroxide and 8 g. of NBS in 400 cc. of carbon tetrachloride was heated on a water bath, protected from moisture. As soon as the boiling took place, the mixture turned red and suddenly the color disappeared. After the boiling was further continued gently for 3 minutes the mixture was cooled under the tap and allowed to stand for 2 hours in a refrigerator. Succinimide was removed and washed with carbon tetrachloride. Carbon tetrachloride solutions were united, washed with 20 cc. of 20% sodium carbonate solution and then with water, and finally dried over anhydrous potassium carbonate. After removal of the solvent, residual oil was distilled in vacuo to yield 5.3 g. (50%) of a slightly colored oil, boiling at 140~145°C/1 mmHg.

Found: N, 5.85. Calcd. for $C_9H_{14}O_3NBr$: N, 5.31%.

A mixture of 0.1 g. of the above oil, 0.1 g. of 2,4-dinitrophenylhydrazine, 3 cc. of ethanol and 0.1 cc. of concentrated hydrochloric acid was boiled on a water bath for 2 minutes and let stand overnight. Crystals formed were recrystallized twice

13) W. S. Johnson and H. Posvic, *J. Am. Chem. Soc.*, **69**, 1361 (1947).

from methanol to yield yellow **2, 4-dinitrophenylhydrazone**, m. p. 149~152°C (decomp.).

Found: N, 15.86. Calcd. for $C_{15}H_{19}O_6N_5Br$: N, 15.75%.

3, 5-Dibromo-1-azacycloheptan-4-one Hydrobromide (XXI).—A solution of 3 g. of X and 15 g. of bromine dissolved in 5 cc. of glacial acetic acid was allowed to stand overnight. The solution was heated on a water bath for 50 hours and evaporated under reduced preseure. The residue was taken up in ethanol, which was evaporated to leave an oil with some crystals. To this was added a small amount of ethanol to bring the oil into solution and isopropyl ether was added in small portions until precipitation occurred. After standing overnight in a refrigerator, the crystals were collected and charcoaled in 200 cc. of ethanol. Charcoal was separated and the ethanolic solution was concentrated to a smaller volume under reduced pressure. The crystals which were deposited during the evaporation were collected and washed with ethanol to yield 0.8 g. of XXI. Another crop, 0.4 g. was obtained from the filtrate. Crude crystals were recrystallized together from a small amount of water to give 0.7 g. of XXI as slightly colored microneedles, m. p. 186°C (decomp.).

Found: C, 20.33; H, 2.89; N, 3.68. Calcd. for $C_6H_9ONBr_2 \cdot HBr$: C, 20.45; H, 2.84; N, 3.97%.

2-Ethoxycarbonyl-2, 3, 4, 5-tetrahydro-1(H)-indolo-[2, 3-c]azepine (XXII).—A mixture of 5.3 g. of XX and 10.6 g. of redistilled aniline was boiled in an oil bath for 3 hours. The reaction mixture was treated with diluted potassium carbonate solution and taken up in ether. Ether was removed and aniline was thoroughly driven off by distillation in an oil bath maintained at 180°C under diminished pressure (0.8 mmHg). The residual tarry oil was dissolved in 70 cc. of benzene and washed once with 5 cc. of 2 N hydrochloric acid, thrice with a small portion of saturated sodium chloride solution and dried over anhydrous potassium carbonate. To the residue left on evaporation of benzene were added ethanol and picric acid, boiled for a while and allowed to stand overnight. Crystals formed were collected, washed with ether and recrystallized from ethanol to yield 1.5 g. (15.3%) of **picrate** as tan needles (indol odor), m. p. 156°C.

Found: N, 14.46. Calcd. for $C_{15}H_{15}O_2N_2 \cdot C_6H_3O_7N_3$: N, 14.37%.

Free base, though in poor yield, was obtained by treating the picrate with a saturated sodium bicarbonate solution and extracting with benzene as extremely viscous yellow oil (indole odor), boiling at 216°C/0.4 mmHg. This did not crystallize on standing.

Found: N, 10.75. Calcd. for $C_{15}H_{19}O_2N_2$: N, 10.85%.

The free base again formed a **picrate** which was found to be the same as that mentioned above, giving no m. p. depression.

2-Ethoxycarbonyl-7-methoxy-2, 3, 4, 5-tetrahydro-1(H)-indolo[2, 3-c]azepine (XXIII) Picrate.—A mixture of 2.8 g. of XX and 3.3 g. of redistilled *p*-anisidine was treated as before and 0.5 g. (9.1%) of picrate (indole odor) was obtained as deep tan needles, m. p. 164.5°C.

Found: N, 13.66. Calcd. for $C_{16}H_{20}O_3N_2 \cdot C_6H_3O_7N_3$: N, 13.54%.

Free base was distilled in vacuo at 220~228°C/0.5 mmHg with decomposition, and for lack of the distillate it could not be studied further.

Deethoxycarbonylation of XXII.—The picrate of XXII, 1 g. was treated with a saturated sodium bicarbonate solution and taken up in benzene. The residual oil which was left on evaporation of benzene was dissolved in 8 cc. of glacial acetic acid and saturated with dry hydrogen bromide under cooling. After standing overnight the solution was boiled under reflux for 2 hours. Acetic acid was removed under reduced pressure and the residue was heated in ethanol with an excessive picric acid. Crystals deposited on standing were recrystallized twice from ethanol to give 0.2 g. of Ia picrate as tan yellow prisms, m. p. 254°C (decomp.).

Found: C, 51.80; H, 4.43; N, 16.65. Calcd. for $C_{12}H_{14}N_2 \cdot C_6H_3O_7N_3$: C, 52.05; H, 4.13; N, 16.86%.

The author wishes to acknowledge the helpful advice of Professor A. Yokoo (this laboratory), and to thank Mr. A. Kondo (the Department of Organic Chemistry, Tokyo Institute of Technology) for carrying out the carbon and hydrogen micro-analyses and Mr. K. Kurosaki (Research Laboratory of Fuji-Photo Film Company) for the infrared measurements and valuable suggestions.

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Studies on Seven-Membered Heterocyclic Compounds Containing Nitrogen. VI. 7-Methyl-2,3,4,5-tetrahydro-1(H)-thiazolo[5,4-c]azepine

By Akira YOKOO and Shiro MOROSAWA

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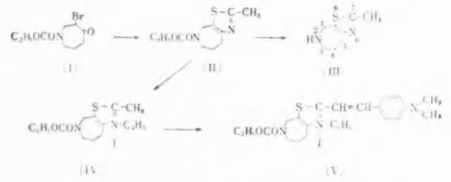
The present authors have synthesized 7-methyl-2,3,4,5-tetrahydro-1-(H)-thiazolo[5,4-c]-azepine (III). Spectral studies also supported the structure.



3-Bromo-1-ethoxycarbonyl-1-azacycloheptan-4-one (I)[1] yielded 2-ethoxycarbonyl-7-methyl-2, 3, 4, 5-tetrahydro-1(H)-thiazolo[5,4-c]azepine (II), b. p. 160~164°C/1 mmHg, by condensation with thioacetamide. II gave a chloroaurate of m. p. 180°C (decomp.). On deethoxycarbonylation of II by hydrogen bromide in glacial acetic acid, III was obtained as an oil of b. p. 101~102°C/4 mmHg, which gave a hydrochloride of m. p. 207~212°C (decomp.) and a chloroaurate of m. p. 179°C (decomp.) respectively. Ethiodide (IV) of II condensed with *p*-dimethylaminobenzaldehyde to afford 2-ethoxycarbonyl-7-(*p*-dimethylaminostyryl)-6-ethyl-2, 3, 4, 5-tetrahydro-1(H)-thiazolo[5, 4-c] azepinium iodide (V), m. p. 203°C (decomp.). Dehydrogenation of III by heating with 10% palladium on carbon at elevated temperature evolved hydrogen, but led to decomposition of III.

It has already been reported[1] that bromine atom entered the 3-position by NBS bromination of 1-ethoxycarbonyl-1-azacycloheptan-4-one and that the indole compounds derived from the consequent bromoketone by the condensation with some arylamines might have angular structures. As shown in Fig. 1, III gave four bands at 1478, 1468, 1455 and 1430 cm^{-1} near the region due to the hydrogen bending vibration of methylene. These bands were assumed, as stated in the former paper[2], to be ascribed to 3-, 1-, 4- and 5-methylenes respectively. It was considered that the intensity of the band at 1455 cm^{-1} was too strong for the methyl group in the thiazole ring and therefore it

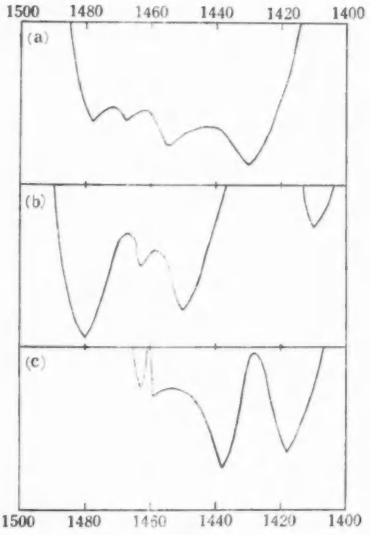


Fig. 1.
(a) III; (b) III hydrochloride;
(c) III hydrobromide

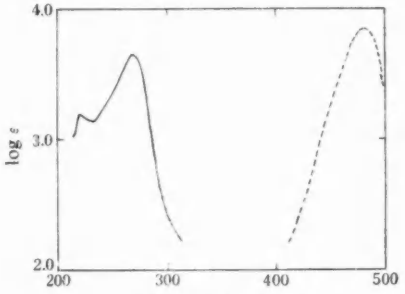


Fig. 2. (in methanol)
—— II, ---- V (concn. unknown)

appeared as an overlapping with 4-methylene. Both hydrochloride and hydrobromide of III gave also four bands, corresponding to the above absorptions. From these facts it may be reasonable to assume that III also had an angular

1) S. Morosawa, This Bulletin, 33, 1113 (1960).
2) S. Morosawa, ibid., 33, 1108 (1960).

form like the compounds reported before[1,2]. Ultraviolet absorption spectra of II and V are also given in Fig. 2.

Experimental

2-Ethoxycarbonyl-7-methyl-2, 3, 4, 5-tetrahydro-1(H)-thiazolo[5, 4-c]azepine (II).—A solution of 5 g. of I and 2 g. of thioacetamide in 15 cc. of ethanol was boiled under reflux on a water bath for 5 hours. The ethanol was removed and the residue was heated in an oil bath kept at 160~165°C under reduced pressure (water pump) for 5 hours. After cooling, 10 cc. of 4 N hydrochloric acid was added and taken up three times in ether. The ether was washed twice with each 5 cc. portion of 4 N hydrochloric acid. Acidic solutions were united and made alkaline with anhydrous potassium carbonate, followed by adding 5 cc. of 5 N sodium hydroxide solution. The alkaline solution was shaken three times with each 20 cc. portion of ether. After drying over anhydrous potassium carbonate, the ethereal solution was concentrated and the residue was distilled in vacuo to give 1.6 g. of a light yellow viscous oil, b. p. 160~164°C/1 mmHg.

Found: C, 54.53; H, 6.74; N, 11.20. Calcd. for $C_{11}H_{16}O_2N_2S$: C, 54.99; H, 6.71; N, 11.65%.

The nitrogen content showed a slightly low value even after several repetitions, and the inclination was also observed in the following compounds of this series.

Ethanolic solution of the oil was mixed with an excessive chloroauric acid, heated for a while and allowed to cool. The **chloroaurate** formed was recrystallized twice from ethanol to yellow crystals, melting at 180°C with decomposition.

Found: C, 22.20; H, 3.33; Au, 32.50. Calcd. for $C_{11}H_{16}O_2N_2S \cdot HAuCl_4$: C, 22.60; H, 2.94; Au, 33.80%.

The oil and an excessive amount of ethyl iodide were allowed to stand for one day. The mixture was then refluxed for 8 hours to form an **ethiodide IV.** It was filtered and recrystallized from ethanol and ether to colorless crystals, m. p. 155~156.5°C.

Found: C, 39.05; H, 5.32; N, 6.39. Calcd. for $C_{11}H_{16}O_2N_2S \cdot C_2H_5I$: C, 39.40; H, 5.34; N, 7.07%.

7-Methyl-2,3,4,5-tetrahydro-1(H)-thiazolo[5,4-c]-azepine (III).—A solution of 0.8 g. of II in 20 cc. of glacial acetic acid was saturated with hydrogen bromide under ice-water cooling. After standing for 2 hours the solution was heated gradually in an oil bath and refluxed for 5 hours. The Hydrobromide which remained as a crystalline residue on evaporation of acetic acid was recrystallized from a mixture of ethanol and methanol to colorless crystals, m. p. 248~252°C (decomp.). These were dissolved in a small amount of water, made alkaline by adding concentrated sodium hydroxide solution and taken up in ether. After drying over anhydrous potassium carbonate, the ether was expelled and the residue was distilled in vacuo to yield 0.4 g. of a colorless, strongly hygroscopic oily substance, b. p. 101~102°C/4 mmHg.

Found: C, 56.60; H, 7.40; N, 16.29. Calcd. for $C_8H_{12}N_2S$: C, 57.14; H, 7.19; N, 16.65%.

The above oil was dissolved in concentrated hydrochloric acid and evaporated to dryness under reduced pressure to afford a **hydrochloride.** This was recrystallized twice from ethanol to extremely hygroscopic colorless plates, m. p. 207~212°C (decomp.).

Found: N, 11.16. Calcd. for $C_8H_{12}N_2S \cdot 2HCl$: N, 11.62%.

The **chloroaurate** which formed by mixing the oil with an excessive amount of chloroauric acid in ethanol containing one drop of concentrated hydrochloric acid was collected and washed with ethanol. This was dissolved in an ethanol-methanol mixed solvent with heating, the methanol was expelled and the solution was allowed to stand with one drop of concentrated hydrochloric acid to yield yellow crystals, which decomposed at about 179°C.

Found: N, 5.06. Calcd. for $C_8H_{12}N_2S \cdot HAuCl_4$: N, 5.50%.

2-Ethoxycarbonyl-7-(*p*-dimethylaminostyryl)-6-ethyl-2, 3, 4, 5-tetrahydro-1(H)-thiazolo[5, 4-c]azepinium Iodide (V).—A solution of 0.1 g. of IV and 0.1 g. of *p*-dimethylaminobenzaldehyde in 2 cc. of ethanol containing a small amount of piperidine was boiled under reflux for 10 hours. The ethanol was expelled and water was added to the residue to deposit crystals, which were collected and washed well with ether. The crystals were dissolved in a small volume of ethanol with heating and ether was added until the solution became turbid. The red crystals which formed were treated repeatedly like the above to give 40 mg. of V, m. p. 203°C (decomp.). The nitrogen content showed some deviation from the theoretical value even after several recrystallizations.

Found: N, 7.01. Calcd. for $C_{22}H_{31}O_2N_3SI$: N, 7.97%.

The authors wish to thank Mr. K. Kurosaki (Research Laboratory of Fuji Photo Film Company) for the infrared measurements and Mr. A. Kondo (the Department of Organic Chemistry, Tokyo Institute Technology) for the carbon and hydrogen micro-analyses.

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The Photolysis of Acetaldehyde in the Presence of Hydrogen Sulfide

By Naomi IMAI and Osamu TOYAMA

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The present authors have recently studied the photolysis of acetone in the presence of hydrogen sulfide in order to obtain information on the hydrogen abstraction from hydrogen sulfide molecules by methyl radicals[1]. The activation energy of the abstraction reaction thus obtained is of such small value that it seems desirable to check it in another way. The present work presents such an attempt on the basis of an investigation on the photolysis of acetaldehyde in the presence of hydrogen sulfide.

We have been interested in this abstraction reaction in conjunction with the mechanism of the thermal decomposition of acetaldehyde in the presence of hydrogen sulfide. The present study is therefore expected to give valuable information also on other elementary reactions involved in common in both kinds of decomposition, photochemical and thermal, in the system consisting of acetaldehyde and hydrogen sulfide.

Experimental

Materials.—Acetaldehyde was prepared by distillation of paraldehyde containing a little quantity of sulfuric acid, and stored in a bulb at 0°C. When the acetaldehyde thus stored was not used at once, it was again purified by distillation befroe use. Hydrogen sulfide was prepared by dropping water on aluminum sulfide in an evacuated vessel, dried by passing through a trap at −78°C and purified by bulb to bulb distillation.

Apparatus.—Photolysis was carried out in a cylindrical quartz vessel of about 110 cc. placed in an electric furnace with a thin glass window which cuts off the light of a wavelength region shorter than 2800 Å to prevent absorption by hydrogen sulfide. The reaction vessel was connected to a mercury manometer, to an analytical system, to storage bulbs and to a bulb in which acetaldehyde and hydrogen sulfide were mixed before they were admitted to the reaction vessel. The full light from a medium pressure mercury arc was used in the present study, and its intensity was kept constant for a series of runs by using a voltage stabilizer. For experiments with varied intensity, the distance between the light source and the reaction vessel was changed. The reaction vessel, the manometer, the bulbs for storage and mixing and the analytical system were all attached to a conventional vacuum line.

Procedure.—Required quantities of acetaldehyde and hydrogen sulfide were admitted into the mixing bulb at room temperature and left for about 30 minutes to allow them to mix thoroughly. The mixed gases were then introduced into the reaction vessel which had already been irradiated, and the change in the total pressure with time was followed on a manometer.

The analytical technique employed was the same as that described previously[1]. In this work the hydrogen sulfide added initially was found by analysis to remain almost unconsumed even after a prolonged photolysis.

Results and Discussion

It has been established by many workers[2] that the products of the photolysis of acetaldehyde above 100°C under normal conditions are almost exclusively methane and carbon monoxide. Similarly in this work, i. e., in the presence of hydrogen sulfide, it has been confirmed by analysis that the rate of formation of methane is identical with that of carbon monoxide, and the pressure of either one of these products corresponds to the total pressure increase within the experimental error. Thus, irrespective of the presence of hydrogen sulfide, the total pressure increase is always equal to the decrease in the pressure of acetaldehyde

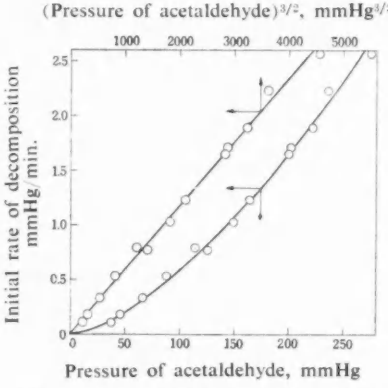

Fig. 1. Rate of decomposition of acetaldehyde alone at 250°C.

1) N. Imai and O. Toyama, This Bulletin, **33**, 652 (1960).

2) F. E. Blacet and D. Volman, *J. Am. Chem. Soc.*, **60**, 1243 (1938); F. E. Blacet and W. J. Blaedel, ibid., **62**, 3374 (1940); R. E. Dodd and J. D. Waldron, *Nature*, **167**, 655 (1951).

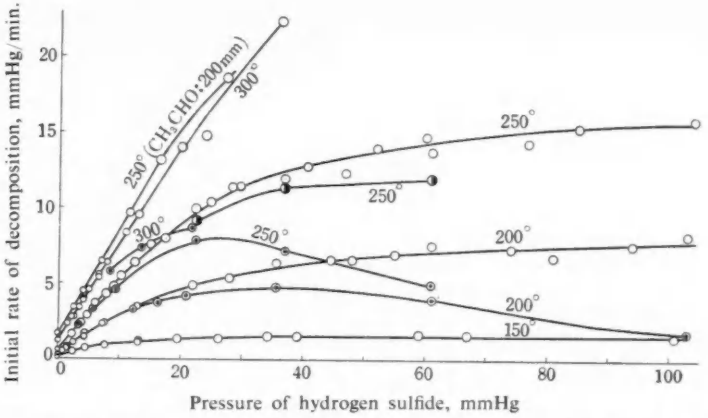

Fig. 2. Dependence of the rate of decomposition in the presence of hydrogen sulfide on its pressure. Relative light intensity: 1. CH_3CHO: 100 mmHg unless otherwise described. ○, without preheating; ◑, with preheating for 1 min.; ⊙, with preheating for 5 min.

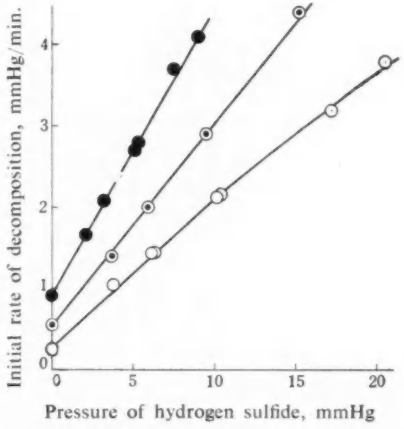

Fig. 3. Dependence of the rate of decomposition in the presence of hydrogen sulfide on its pressure. Relative light intensity: 1/4. CH_3CHO: 100 mmHg, ○, 250°; ⊙, 300°; ●, 360°C. All the data were obtained without preheating.

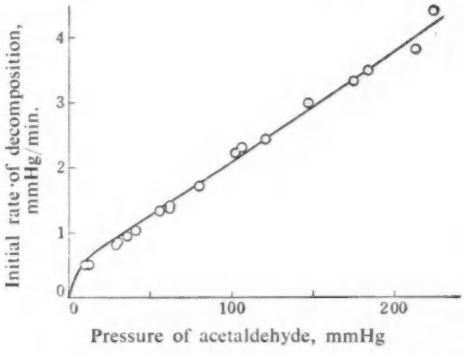

Fig. 4. Dependence of the rate of decomposition in the presence of hydrogen sulfide on acetaldehyde pressure. Temperature: 250°C. H_2S: 3.16 mmHg. Circles and full line represent observed and calculated rates respectively.

due to decomposition. Accordingly, the initial rate of decomposition was determined from the initial slope of a total pressure-time curve with the results shown in Figs. 1—4. Fig. 1 shows the dependence of the rate of decomposition on the pressure of acetaldehyde in the experiments with acetaldehyde alone. Figs. 2 and 3 show the dependence of the rate of decomposition in the presence of hydrogen sulfide on its pressure under various experimental conditions. The relative light intensity intensity for the experiments shown in Fig. 2 is four times as great as that in Fig. 3. Fig.

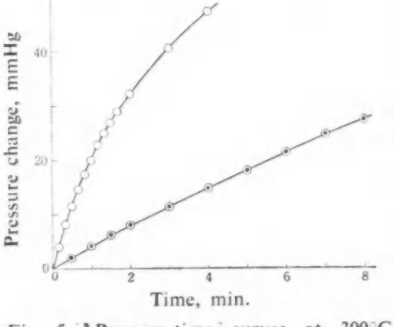

Fig. 5. Pressure-time curves at 300°C. Initial pressure: CH_3CHO, 100 mmHg. H_2S, ⊙, 3.5; ○, 36.2 mmHg.

4 shows the dependence of the rate on acetaldehyde pressure in the presence of hydrogen sulfide.

It should be noted that, at a high temperature, in a run with a high concentration of hydrogen sulfide, the rate of decomposition falls off very rapidly, as seen in Fig. 5, compared to the results obtained with low concentrations of hydrogen sulfide. Similar reduction in the rate was observed, as seen in Fig. 2, when the acetaldehyde mixed with a large quantity of hydrogen sulfide was preheated for a few minutes at the experimental temperature prior to irradiation. Although the exact nature of these phenomena has not yet been fully elucidated, it is obvious from these findings that at still higher concentrations of hydrogen sulfide than those given in Fig. 2, determination of the initial rate of decomposition becomes considerably unreliable.

It is generally agreed that the main features of the photochemical decomposition of acetaldehyde can be explained by the following mechanism[3]:

$$CH_3CHO + h\nu = CH_3 + CHO \quad (0)$$

$$CHO = CO + H \quad (1)$$

$$H + CH_3CHO = H_2 + CH_3CO \quad (2)$$

$$CH_3CO = CH_3 + CO \quad (3)$$

$$CH_3 + CH_3CHO = CH_4 + CH_3CO \quad (4)$$

$$CH_3 + CH_3 = C_2H_6 \quad (5)$$

Solution of the steady state equations derived from this scheme yields the rate equation (I_a = the rate of absorption of light quanta)

$$-\mathrm{d}[CH_3CHO]/\mathrm{d}t = k_1 k_5^{-1/2} I_a^{1/2} [CH_3CHO] \quad (I)$$

in general agreement with experimental results obtained by various workers. The existence of a primary reaction other than reaction (0) is well known[4]. This, however, gives no substantial alteration in Eq. I. From the plot given in Fig. 1 it is seen that the rate of decomposition of acetaldehyde alone is proportional to the 3/2 power of its pressure. This simply means that under the present experimental conditions the rate of absorption of light quanta is proportional to the acetaldehyde pressure.

Now in the presence of hydrogen sulfide, the possible additional reactions may be[5]

$$CH_3 + H_2S = CH_4 + HS \quad (6)$$

$$HS + CH_3CHO = H_2S + CH_3CO \quad (7)$$

$$HS + HS = \text{products} \quad (8)$$

If reaction (8) can be neglected and consequently the chain terminates still by reaction (5),

$$-\mathrm{d}[CH_3CHO]/\mathrm{d}t = k_1 k_5^{-1/2} I_a^{1/2} [CH_3CHO] + k_6 k_5^{-1/2} I_a^{1/2} [H_2S] \quad (II)$$

while, if the chain terminates now by reaction (8), the result is

$$-\mathrm{d}[CH_3CHO]/\mathrm{d}t = k_7 k_8^{-1/2} I_a^{1/2} [CH_3CHO] \quad (III)$$

It is readily shown that in the steady state,

$$k_6 [CH_3] [H_2S] = k_7 [HS] [CH_3CHO]$$

or

$$[HS]/[CH_3] = (k_6/k_7)([H_2S]/[CH_3CHO])$$

Therefore, when the value of $(k_6/k_7)([H_2S]/[CH_3CHO])$ is very small, i.e., the concentration of methyl radical is much higher than that of hydrosulfide radical, the rate of decomposition will be represented by Eq. II. On the contrary, when the value of $(k_6/k_7)([H_2S]/[CH_3CHO])$ is very large, Eq. III will hold.

In Figs. 2 and 3 where the rates of decomposition are plotted against pressures of hydrogen sulfide, it is seen that, in the low pressure range of hydrogen sulfide, except for the experiments with preheating, the rate of decomposition increases linearly with the pressure of hydrogen sulfide in agreement with Eq. II. The fact that the intercept on the ordinate is always equal to the rate of decomposition in the absence of hydrogen sulfide also conforms to Eq. II. According to the equation the slope of the linear part divided by the intercept gives the ratio k_6/k_4. The values of k_6/k_4 thus

TABLE I. VALUES OF k_6/k_4

Initial pressure of CH_3CHO: 100 mmHg

Temp. °C	Relative light intensity = 1	Relative light intensity = 1/4
200	115	
250	78.7	75.5
	82.0[a]	
300	55.2	54.1
360		38.6

a) Initial pressure of CH_3CHO: 200 mmHg.

3) E. I. Akeroyd and R. G. W. Norrish, *J. Chem. Soc.*, **1936**, 890; J. A. Leemakers, *J. Am. Chem. Soc.*, **56**, 1537 (1934); D. C. Grahame and G. K. Rollefson, *J. Chem. Phys.*, **8**, 98 (1940); C. J. Darby, A. S. Buchanan and I. H. S. Henderson, *J. Chem. Soc.*, **1951**, 1426.

4) (a) F. E. Blacet and D. E. Loeffler, *J. Am. Chem. Soc.*, **64**, 893 (1942). (b) M. A. Khan, R. G. W. Norrish and G. Porter, *Proc. Roy. Soc.* (*London*), **A219**, 312 (1953). (c) P. P. Manning, *J. Am. Chem. Soc.*, **79**, 5151 (1957). (d) R. E. Dodd, *Can. J. Chem.*, **33**, 699 (1955).

5) Similar reactions have been proposed by the following workers: (a) E. F. P. Harris and W. A. Waters, *Nature*, **170**, 212 (1952); (b) K. E. J. Banett and W. A. Waters, *Disc. Faraday Soc.*, **14**, 221 (1953); (c) R. N. Birrell, R. F. Smith, A. F. Trotman-Dickenson and H. Wilkie, *J. Chem. Soc.*, **1957**, 2087.

determined are listed in Table I[6]. The fact that neither a two-fold increase in the pressure of acetaldehyde, nor the variation in light intensity by a factor of four, yields any significant change in the values of k_6/k_4 may be taken as additional evidence for the validity of Eq. II.

A further check in favor of Eq. II is provided by Fig. 4, where the plot of the rates of decomposition observed at a constant pressure of hydrogen sulfide against acetaldehyde pressures is shown together with the curve predicted from Eq. II as follows: Since the rate of absorption of radiation in the present investigation is proportional to the concentration of acetaldehyde as mentioned above, the values of $k_4k_5^{-1/2}I_a^{1/2}$ and $k_6k_5^{-1/2}I_a^{1/2}$ required for the calculation of the rate of decomposition by means of Eq. II can be obtained from the data given in Figs. 1 and 2. As seen in Fig. 4, the curve representing the rate thus calculated as a function of acetaldehyde pressure is in satisfactory agreement with the experimental plot over a wide range of acetaldehyde pressure.

The Arrhenius plots of the values of k_6/k_4 given in the two series in Table I yielded two parallel straight lines lying close to each other from which the values $E_4-E_6=4.0\pm0.3$ kcal./mol. and $A_6/A_4=1.7\pm0.5$ were obtained, where E denotes the activation energy and A the pre-exponential factor. The ratio $A_6/A_4=1.7$ seems to be reasonable since A factors for most hydrogen abstraction reactions by methyl radicals are of the same order of magnitude. The activation energy difference $E_4-E_6=4.0$ kcal./mol., when combined with $E_4=6.8$ kcal./mol. given by Ausloos and Steacie[7], yields 2.8 kcal./mol. for E_6 which compares satisfactorily with our previous value of 2.6 kcal./mol. obtained in the photolysis of acetone in the presence of hydrogen sulfide[1]. If, instead, $E_4=7.5\sim8.0$ kcal./mol. reported by Brinton and Volman[8] and Dodd[4d] is accepted, the result is $E_6=3.5\sim4.0$ kcal./mol. which is now clearly higher than the previous value but still lower than 5.6 kcal./mol.[9] estimated for the activation energy of hydrogen abstraction from methane thiol by methyl radical, in agreement with our previous conclusion[1].

It is evident from Figs. 2 and 3 that, for the experiments without preheating, the lower the temperature, the lower is the pressure of hydrogen sulfide at which a plot of the rate of the decomposition against the pressure of hydrogen sulfide shows a departure from a straight line. At a temperature as low as 150°C, the plot (Fig. 2) shows a curvature from the very beginning and, in the range of pressure of hydrogen sulfide higher than about 30 mmHg the rate of decomposition attains an almost constant value in agreement with Eq. III.

Presumably, these fact indicate that the ratio k_6/k_7 increases with lowering of temperature, for, with the increase in the ratio k_6/k_7, $[CH_3]/[HS]$ and hence the ratio of the rate of reaction (8) to that of reaction (5) increases, provided the ratio $[H_2S]/[CH_3CHO]$ is constant. Such dependence of the ratio k_6/k_7 on temperature seems to be reasonable since the activation energy for reaction (6) is very low as estimated above so that it is probably lower than that of reaction (7).

The afore-mentioned observation that, in the presence of a large concentration of hydrogen sulfide, the rate of photolysis suffered considerable reduction not only by preheating the reaction mixture, but also during the photolysis at a high temperature, cannot fully be explained at present. It may, however, be possible that a small quantity of a yet unidentified compound produced in the thermal reaction between acetaldehyde and hydrogen sulfide gives rise to the observed phenomena. Birrell et al.[9c] found that the rate of decomposition of acetaldehyde is reduced appreciably by large quantities of isopropanethiol and tertiary-butanethiol below 300°C, and to almost negligible values by small quantities of tertiary-butanethiol and isopropanethiol above 300°C and 340°C respectively. We have also found[10] that the presence of a little quantity of methanethiol lowers remarkably the rates of photolyses of acetone, acetaldehyde and a mixture of acetaldehyde and hydrogen sulfide. In view of the similarity of the phenomena cited, it seems probable that all of these resulted from similar causes which, however, are to be clarified by further studies of these phenomena in future.

Summary

Acetaldehyde has been photolyzed in the presence of hydrogen sulfide over the temperature range from 150 to 360°C. The initial rates of decomposition obtained under various experimental conditions are consistent with a mechanism which involves the reactions $CH_3+H_2S=CH_4+HS$ (6) and $HS+CH_3CHO=H_2S+CH_3CO$ (7) in addition to those established already for the photolysis of acetaldehyde alone. Analysis of the data on this basis gives

6) The value of the intercept was actually determined from several repeated runs of the photolysis of 100 mmHg acetaldehyde in the absence of hydrogen sulfide at the same temperature.

7) P. Ausloos and E. W. R. Steacie, *Can. J. Chem.*, **33**, 31 (1955).

8) D. H. Volman and R. K. Brinton, *J. Chem. Phys.*, **20**, 1764 (1952).

9) T. A. Kerr and A. F. Trotman-Dickenson, *J. Chem. Soc.*, **1957**, 3322.

10) N. Imai and O. Toyama, unpublished work.

a value of 4.0 kcal./mol. for the difference in activation energy $E_4 - E_6$, where E_4 refers to the reaction $CH_3 + CH_3CHO = CH_4 + CH_3CO$ (4). This result, when combined with $E_4 = 6.8$ kcal./mol. found by Ausloos and Steacie, gives $E_6 = 2.8$ kcal./mol. in excellent agreement with our previous value of 2.6 kcal./mol. obtained in the photolysis of acetone in the presence of hydrogen sulfide. As the temperature is lowered and the ratio $[H_2S]/[CH_3CHO]$ increased, the importance of the combination of methyl radicals to ethane as the chain terminating step decreases, until it is replaced by the combination of hydrosulfide radicals. This is explained in terms of the relationship $E_7 > E_6$.

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Alternating Current Polarization Titration with Two Hanging Mercury Drop Electrodes—Application to Chelatometric Titration of Cadmium

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Both potentiometry at a constant current and amperometry at a small constant applied voltage with two polarized platinum electrodes are widely used for the determination of the equivalent point in a large number of titrations. The relation between the two methods of titration mentioned above has been recently discussed by several authors on the basis of voltammetry[1-4].

On the other hand, conductometric titration using low frequency of 200~1000 c/sec. has been applied to the determination of the equivalent point in titrations involving acid-base neutralization reaction or precipitation reaction. However, alternating current polarization titration, which corresponds to the alternating current analogs of the two direct current method, situated between direct current polarization titration and conductometric titration has not been studied systematically. Recently Franck[5], Laitinen[6] and the present author[7] studied these methods, and applied them to redox, precipitation and complex formation reaction.

The present author studied polarization titration fundamentally, applying to a pair of platinum microelectrodes a square wave or sine wave signal of constant current and measuring the alternating voltage (polarization voltage) in the course of a titration.

This is a suitable method which can be applied in redox reaction, complex formation reaction and neutralization reaction. It is impossible, however, that metal ion concentration is indicated by the platinum electrode, except in the case of some reversible system; for example, ferric-ferrous system. Hence when the chelatometric titration of metal ion is carried out by the polarization titration method, an excess of ethylenediaminetetraacetate (EDTA) solution of a known concentration is added, and the excess of EDTA is back-titrated with standard ferric solution. However, when the stability constant of metal ion titrated is much smaller than that of ferric ion, this titration method can not be used. Accordingly, only a few kinds of metal ion, ferric, indium and nickel, are titrated by this method[8]. For this reason, it seemed desirable and worth while to investigate the chelatometric titration of most metal ions by alternating current polarization titration with two mercury drop electrodes.

In this paper, the experimental results of the application to the cheltometric titration of the cadmium ion are presented, and the factors which affect this titration method are discussed.

1) R. Gauguin, *Anal. Chim. Acta*, **5**, 200 (1951); **7**, 172, 360, 408 (1952).
2) I. M. Kolthoff, *Anal. Chem.*, **26**, 1685 (1954).
3) M. Ishibashi and T. Fujinaga, *J. Electrochem. Soc. Japan* (*Denkikagaku*), **23**, 494 (1955).
4) N. Tanaka, *Japan Analyst* (*Bunseki Kagaku*), **4**, 640 (1955).
5) U. F. Franck, *Z. Elektrochem.*, **58**, (1954).
6) H. A. Laitinen and L. C. Hall, *Anal. Chem.*, **29**, 1390 (1957).
7) T. Kitagawa, *Bulletin of the Faculty of Education, Kobe University* (*Kobedaigaku Kyōikugakubu Kenkyushuroku*), **21**, 29 (1959).
8) T. Kitagawa, *Bulletin of the Faculty of Education, Kobe Univrsity* (*Kobedaigaku Kyōikugakubu Kenkyushuroku*), **21**, 39 (1959).

Experimental

Reagents.—A standard EDTA solution was obtained by dissolving the pure disodium ethylenediaminetetraacetate dihydrate (Wako Junyaku Co. Ltd.) in distilled water. The concentration was standardized against a standard copper solution by photometric titration using Murexide as indicator. The concentration was 0.100 M. A 0.01 M EDTA solution was prepared by dilution. Standard cadmium solution was prepared by dissolving cadmium nitrate in distilled water. The concentration was determined gravimetrically as cadmium oxinate. Standard mercuric ethylenediaminetetraacetate was prepared by mixing equivalent amounts of mercuric nitrate solution and EDTA solution. The concentration was 0.05 M.

All other chemicals were of analytical reagent grades. Redistilled water was used for the preparation of the solutions.

Apparatus.—Alternating current polarization titration apparatus is shown in Fig. 1. Kikusui Type CR oscillator was used for sine wave or square wave generator (20～2000 c/sec.). The circuit of measuring polarization voltage is shown in Fig. 2.

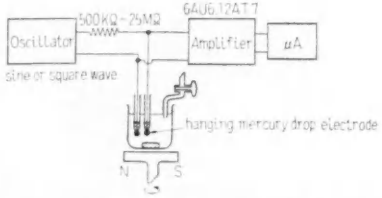

Fig. 1. Alternating current polarization titration apparatus.

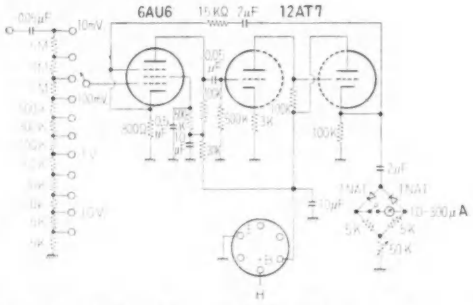

Fig. 2. Circuit of measuring polarization voltage.

The measurement was made at a small current using a large resistor in series with the electrolytic cell and an output voltage (12 volt) from the sine wave or square wave generator. The alternating voltage (polarization voltage) between two electrodes was measured as a function of the volume of reagent added.

The mercury drop electrode was prepared by fixing the mercury drop on the top of amalgamated platinum electrodes. Mercury can be deposited on the platinum electrode out of 1 M mercuric nitrate solution by the impression of an electromotive force of about 2 V. The surface area of the mercury drop was about 0.021 cm^2. A calibrated semimicroburet 5 ml. was used for all titrations.

Procedure.—About 50 ml. of the solution, which contained definite amounts of cadmium nitrate solution, 50 ml. of 1 M ammoium acetate-acetic acid buffer solution (pH 4.3～5.0), 1 ml. of 0.1% gelatine and 10 ml. of 0.05 M mercury (II) EDTA solution, was titrated with 10^{-1} or 10^{-2} M standard solution of EDTA. The frequency of square wave or sine wave was 25 c/sec. and the alternating current was 20～25 μA*. The polarization voltage was recorded at every 0.01 ml. of added titrant in the neighborhood of the equivalence point of this titration.

An example of this titration curve is shown in Fig. 3. In the course of this titration, the solution was stirred at a constant speed by a magnetic stirrer.

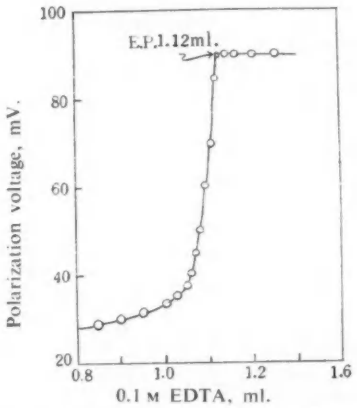

Fig. 3. Titration curve. Cd^{2+} 12.5 mg.

Results

In the procedure described above, the following factors were specially considered.

1) Relation between Polarization Voltage and Frequency.—Polarization voltage was measured at the equivalence point by the procedure described above. As shown in Fig. 4, a plot of polarization voltage against the reciprocal of square root of frequency gives a straight line at frequency 20～200 c/sec. Therefore, the frequency 20 c/sec. was used as a suitable frequency in this titration. In a frequency above 500 c/sec. it was impossible to apply this end point detection method, because the polarization voltage became very small.

2) Relation between Polarization Voltage and Alternating Current.—In the potentiometry at a constant direct current, the difference in potential between two identical indicator

* Calculated value $12(V) \div 500(K\Omega) = 24(\mu A)$

electrodes becomes more extended with the increase of the current[2-4]. On the other hand, polarization voltage at alternating current polarization titration is proportional to the alternating current as shown in Fig. 4. Therefore, 25 μA was used for the suitable alternating current in this titration. If the alternating current becomes very small, it is impossible to use this titration method owing to the decrease of the polarization voltage.

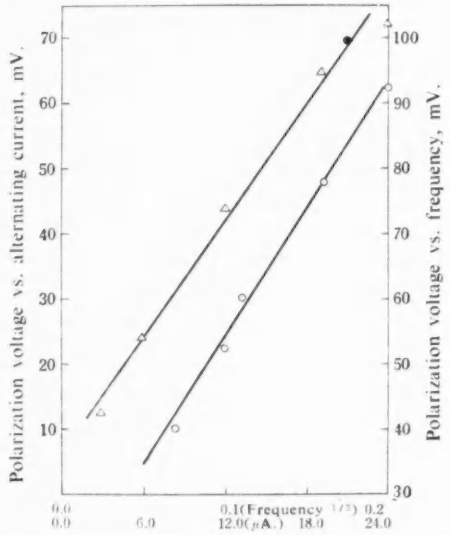

Fig. 4. A) Relation between polarization voltage and frequency (-○-).
B) Relation between polarization voltage and alternating current (-△-).

3) Effect of Surface Area of Mercury Drop.—The polarization voltage became smaller with the increase of the surface area of mercury drop as shown in Fig. 5. However, the area of the mercury electrode gave no effect on the experimental result. The pretreatment of the mercury electrode had also little effect on the shape of this titration curve and on the experimental results. Therefore, alternating current polarization titration has advantages in this point over the direct current polarization titration.

4) Effect of Gelatine.—In chelatometric titration of cadmium using potentiometry at a constant current and amperometry at a constant potential, the addition of gelatine was necessary[9] in order to suppress the kinetic current due to the dissociation of Cd-EDTA. Experimental results in the presence or the absence

9) N. Tanaka et al., *Japan Analyst (Bunseki Kagaku)*, **6**, 86 (1957).

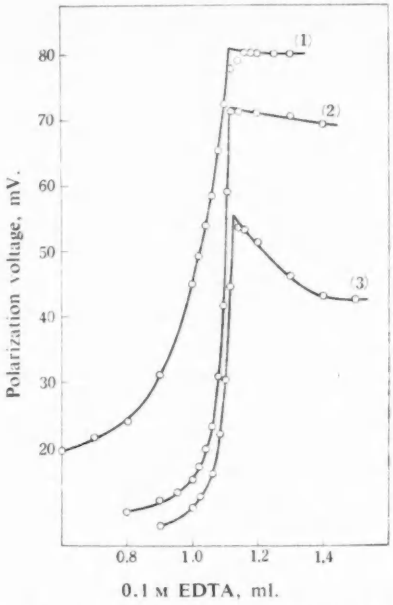

Fig. 5. Effect of surface area of mercury drop.
(1) surface area about 0.02 cm²
(2) 〃 0.03 cm²
(3) 〃 0.05 cm²

of gelatine in this method are shown in Table I. Although experimental results are not reproducible in the absence of gelatine, it is clear that the reproducible and precise results are obtained in the presence of gelatine. Therefore, the addition of 1 ml. of 0.1% gelatine is indispensable in this titration.

TABLE I. EFFECT OF GELATINE ADDED

Cd taken mg.	0.1% Gelatine added ml.	Volume of 10^{-1}M EDTA titrated ml.	Cd found mg.
6.29	0	0.55_0	6.18
6.29	0	0.53_5	6.01
6.29	0	0.55_5	6.18
6.29	0.2	0.55_5	6.24
6.29	0.5	0.56_0	6.28
6.29	1.0	0.56_0	6.28
6.29	2.0	0.56_0	6.28

5) Effect of Wave Form.—The Effect of wave form to this titration (sine wave or square wave) was examined. Although polarization voltage was greater in the case of using sine wave than square wave, it was recognized that the wave form gave little effect on the experimental results.

6) Effect of Hg-EDTA Added.—To determine the optimum amount of Hg-EDTA to be added,

various volumes of the Hg-EDTA solution were added to a constant volume of cadmium nitrate solution. In this case, all other conditions were kept constant according to the procedure described above. The results are shown in Table II. It was found that the amount of the reagent did not affect the determination of cadmium provided that it ranged from 5 to 15 ml.

Table II. Effect of Hg-EDTA added

Cd taken mg.	0.05 M Hg-EDTA added ml.	Volume of 10^{-1} M EDTA titrated ml.	Cd found mg.
12.58	0	1.11_0	12.48
12.58	1	1.12_0	12.56
12.58	2	1.12_5	12.60
12.58	3	1.12_0	12.56
12.58	4	1.12_5	12.60
12.58	5	1.12_5	12.60
12.58	10	1.12_0	12.56
12.58	15	1.12_5	12.60

7) *The Optimum Conditions for the Above-mentioned Procedure.*—They have been concluded as follows: frequency, 20~50 c/sec.; alternating current, 20~25 μA., gelatine, 0.1% 1 ml.; pH of titration solution, 4.3~5.0; the amounts of Hg-EDTA, 10 ml.

8) *Determination of Various Concentrations of Cadmium under the Optimum Conditions.*—Various concentrations of cadmium ions were determined by the procedure described above under the optimum conditions and the results are shown in Table III.

Table III. Determination of various concentrations of Cd^{2+} at the optimum conditions

Cd taken mg.	Volume of EDTA titrated ml.	Cd found mg.	error %
	10^{-1} M EDTA		
12.58	1.12_0	12.56	−0.2
	1.12_5	12.60	+0.2
	1.12_5	12.60	+0.2
6.29	0.56_0	6.28	−0.2
	0.55_5	6.24	−0.9
	0.55_5	6.24	−0.9
	10^{-2} M EDTA		
0.62	0.55_5	0.62	−0.9
	0.55_5	0.62	−0.9
	0.55_5	0.62	−0.9

Discussion

Before the titration is initiated, some of the mercury(II) is displaced from its Hg-EDTA complex by the cadmium ion. The following substitution reaction occurs in the solution[10]

$$HgY^{2-} + Cd \text{ acetate} \rightarrow Hg \text{ acetate} + CdY^{2-}$$

In this case, complete substitution of the Hg-EDTA by the cadmium ion to be titrated is not necessary for successful titration. The end point of chelatometric titration of the cadmium ion in this procedure will be indicated by the change of polarization voltage based on the change of the mercuric ion concentration in the neighborhood of the end point. Accordingly, most metal ions will be titratid by this titration method using suitable solution conditions.

The principle on which alternating current polarization titration is based is the same as that of the direct current method. However, this is a more suitable method than the direct current polarization method in the point that the pretreatment of the mercury drop electrode is not necessary.

Summary

Cadmium was titrated with the EDTA by the alternating current polarization titration with two hanging mercury electrodes and the factors which affect this titration were examined. As a result, it is clear that the end point is indicated by the change of the mercuric ion con centration in the neighborhood of equivalence point. Pretreatment of the mercury drop electrode is not necessary. By this method, cadmium of 10^{-2}~10^{-3} M were titrated with a relative error of 0.9%.

The author wishes to express his hearty thanks to Professor M. Ishibashi, Assistant Professor T. Fujinaga, University of Kyoto, and Assistant Professor H. Hayakawa, University of Kobe, for their encouragement throughout this investigation.

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10) A. E. Martin and C. N. Reilly, *Anal. Chem.*, **31**, 993 (1959).

High Resolution Nuclear Magnetic Resonance Spectra of Ring Protons in Substituted Benzenes

By Ichiro YAMAGUCHI and Naohiro HAYAKAWA

(Received February 16, 1960)

The electron distribution on the benzene ring has been considered to be a very interesting object by many organic chemists, especially with respect to the correlation with the reactivity of the molecule. An experiment of approach to this problem was carried out by Gutowsky and his coworkers[1]. They measured the fluorine nuclear magnetic resonance in a number of fluorobenzenes and investigated the effect of substituents on the fluorine resonance shift and found the correlations between the values of the Hammett σ constant and of the resonance shift. Recently, Bothner-By and Glick[2] and also Corio and Dailey[3] observed the proton resonance spectra of benzene derivatives and discussed the electron densities on the *o*-, *m*- and *p*- protons. The patterns of the proton resonance spectra obtained by them are simple and not adequate for the precise examination of the electron distribution in the benzene derivative molecules. Patterns simpler than the expected ones are mainly due to the fact that the resonance frequency of the experiments was as low as 30 Mc.

Hence, we planned to investigate the proton resonance spectra of the benzene ring protons of a variety of benzene derivatives at 56.4 Mc. This paper reports the results of the analysis of their spectra, and the spectra of disubstituted benzenes are discussed with correlation to the substituents.

Experimental

The Varian High Resolution NMR Spectrometer was operated at 56.4 Mc. The resolution of the apparatus was higher than 10^{-8} when the sample was spun.

The samples measured were of commercial guaranteed grade, and these were used without further purification. The spectra of the liquid samples were taken in pure liquid state. Most of the solid samples were dissolved in acetone to make saturated solutions, and the spectra were taken. The others were dissolved in ethanol or ether.

All of the NMR measurements were carried out at 20°C for the samples sealed in glass tubes with the outer diameter of 5 mm. The spectra were recorded by the Sanborn Recorder and the separations of the resonance peaks were measured on the recorded charts. The magnetic field was swept in both decreasing and increasing directions and the measurements were made by taking the average of the records of both directions of the sweep. The calibration of the sweep rate was made by recording the spectrum of the methylene group of ethanol and by reading the separation of the two highest peaks as 7.0 cps[4]. The sweep rate was about 1 cps/sec.

The chemical shift of the ring proton resonance referred to benzene ring proton was determined for several compounds by adding a small amount of benzene to the sample liquid as an internal standard. This method was found to be inadequate for the precise determination of the shift value, because it was noticed that an additive shift arose by the addition of benzene. Therefore the observed values of the shift referred to benzene, δ_B, include an error of about ± 0.05 p.p.m.

The experimental error over the entire measurements was about 3%. This arose mainly from the instability of the field sweeping of the spectrometer.

Analysis of the Spectra

The systems of the ring protons of benzene derivatives are represented as in Table I, according to the notation proposed by Bernstein et al.[5]. In these systems, the spectra with simple structure may be analyzed by solving the equations of the Hamiltonian of the nuclear spin system and the assignment of the spectral lines can be made. The ratio $J/\nu_0\delta$, where J and $\nu_0\delta$ are respectively the spin coupling constant and the chemical shift in cps between the two resonating nuclei, ranges from 0.2 to more than 1 in the case of benzene ring protons, and in some cases the chemical shift is very small compared with the values of the spin coupling constant. This should be noted when the analysis is made by any approximate method which neglects higher order perturbation terms or some coupling constants.

For each system of ring protons the appropriate approximation method was adopted to

1) H. S. Gutowsky, D. W. McCall, B. R. McGarvey and L. H. Meyer, *J. Am. Chem. Soc.*, **74**, 4809 (1952).
2) A. A. Bothner-By and R. E. Glick, ibid., **78**, 1071 (1956).
3) P. L. Corio and B. P. Dailey, ibid., **78**, 3043 (1956).
4) Varian Assoc., "Technical Information Bulletin", No. 11-2.
5) H. J. Bernstein, J. A. Pople and W. G. Schneider, *Can. J. Chem.*, **35**, 65 (1957).

TABLE I. PROTON GROUPINGS IN SUBSTITUTED BENZENES

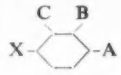
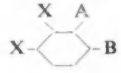
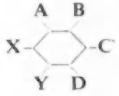
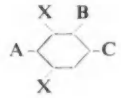
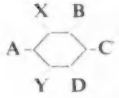
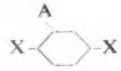
Mono-X benzene	AB_2C_2				
o-Di-X benzene	A_2B_2		*o*-XY benzene	ABCD	
m-Di-X benzene	AB_2C		*m*-XY benzene	ABCD	
p-Di-X benzene	A_4		*p*-XY benzene	A_2B_2	

TABLE II. SPREADING RANGE OF PROTON RESONANCE LINES OF MONO-SUBSTITUTED BENZENES (in cps at 56.4 Mc)

Nitrobenzene	55	Bromobenzene	35
Benzaldehyde	40	Iodobenzene	50
Toluene	Single peak	Aniline	55
Chlorobenzene	22		

analyze the spectrum. In the system of *o*-di-X benzene, the result of the analysis of *o*-dichlorobenzene, obtained by solving the secular equation by Pople et al.[6] was adopted. In *m*-di-X benzene the calculation based on the second order perturbation theory could be adopted for molecules where the ratios $J/\nu_0\delta$ in the molecule are comparatively small. In *p*-XY benzene, the secular equation of the system was solved by neglecting the spin couplings between the protons in *m*-position and in *p*-position to each other[7]. In each case of analysis, the coupling constants between protons are assumed to have positive sign.

Results and Discussion

Monosubstituted Benzene. — The spectra of monosubstituted benzenes are generally very complicated ones and none of the spectral lines can be assigned completely by a simple glance of the structure of the spectra. The preliminary analysis of the spectrum of this system shows that the line groups of *o*-, *m*- and *p*-protons have many lines and each of these spreads over a wide range. In most cases, the *m*- and *p*-protons are overlapping each other as the result of the couplings of protons where the chemical shifts are very small. This chemical shift is, in certain cases, much smaller than the coupling constant between the protons concerned. In addition to this, the spreading range of the resonance lines of *p*-protons is generally wide compared to that of *m*-protons. This makes the assignment of the ring proton spectral lines of monosubstituted benzene very difficult.

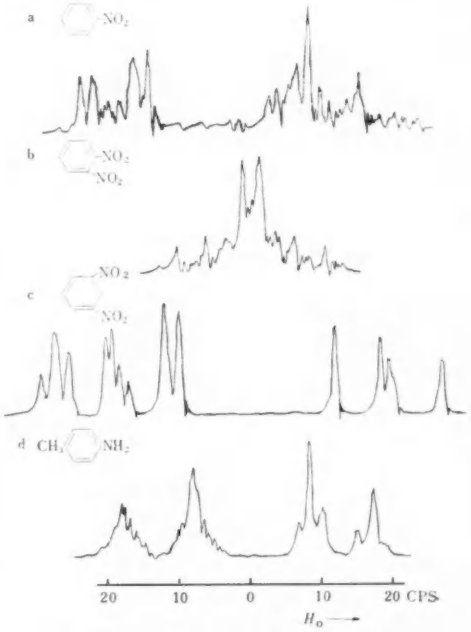


Fig. 1. NMR spectra of ring protons in mono- and di-substituted benzenes.

6) J. A. Pople, W. G. Schneider and H. J. Bernstein "High Resolution Nuclear Magnetic Resonance", McGraw-Hill Book Co., New York (1959), pp. 145-149.

7) R. E. Richards and T. P. Schaefer, *J. Mol. Spectroscopy*, **2**, 1280 (1958).

compared with the other symmetrical systems. Though the spectra of the system reported by Corio and Dailey[3] are relatively simple, the simple spectra are due to the low resonance frequency of their experiment. It seems that the values of chemical shift reported by them may have errors as the result of the fact that the spectral patterns are not well resolved. An example of the spectrum of monosubstituted benzene is shown in Fig. 1a. The range of the spreading of the spectral lines is also shown in Table II. The spreading electron-range of the spectrum is wider as the releasing or withdrawing power of the substituent is stronger.

Disubstituted Benzene.—*o-Di-X Benzene.*—An example of the spectrum of the system is is shown in Fig. 1b. The spectrum spreads in a rather narrow range showing a symmetrical pattern. The magnitudes of the chemical shift and the spin coupling constants are listed in Table III. Generally, the chemical shift between A and B groups of protons is very small and this shows that the difference of the resultant electronic effects of the substituent on the protons of A and B groups is very small.

The chemical shift of the ring proton resonance referred to the benzene ring proton may be considered to arise from two origins. One is variation in the ring current and the other that in the electronic shielding of the protons affected by the substituent. The ring current variation might cause the shift of the whole spectrum in either direction according to whether the ring current density increases or decreases. On the other hand, electronic effects of the substituent would affect the protons at different positions separately by its inductive and resonance effects and the scectral figure would vary according to the difference in the effect on different protons.

For all *o*-di-X benzenes observed, the spectral lines spread almost in similar magnitude while the variety in $\tilde{\sigma}_B$ is rather remarkable. This result would lead to the conclusion that the ring current is considerably affected by the substituent. The same consideration will be held for the other proton systems.

m-Di-X Benzene.—The spectrum of this system is characterized by its three-group pattern as illustrated in Fig. 1c. The last column in Table IV shows the arrangement of spectral line groups in increasing field direction. The order of arrangement of these groups in the spectrum is understood mainly in terms of the electron-releasing and withdrawing power of the substituent X. The resonance position of the A proton is greatly influenced by the electronic nature of the substituent because the position of the proton is between two X's,

TABLE III. CHEMICAL SHIFT AND COUPLING CONSTANT IN *o*-di-X BENZENES
(in cps at 56.4 Mc)

Compound	Solvent	$\nu_0\tilde{\sigma}_{AB}$	J_{AB}	$J_{AB'}$	$J_{BB'}$	$\tilde{\sigma}_B$ (in p.p.m.)
o-Dinitrobenzene	Acetone	7.1	8.4	0.9	3.1	−0.74
Phthalic acid	Acetone	9.3	7.8	0.5	4.1	−0.35
o-Xylene	—	0.0				
o-Dichlorobenzene	—	13.8	8.4	1.9	6.9	+0.24
Catechol	Acetone	11.2	8.1	1.3	5.0	+0.43

TABLE IV. CHEMICAL SHIFT AND COUPLING CONSTANT IN *m*-di-X BENZENES
(in cps at 56.4 Mc)

Compound	Solvent	$\nu_0\tilde{\sigma}_{AB}$	$\nu_0\tilde{\sigma}_{BC}$	J_{BC}	J_{AB}	J_{AC}	Spectrum
m-Dinitrobenzene	Acetone	12.6	33.0	7.6	2.0	0.5	A-B-C
Isophthalic acid	$(CH_3)_2SO$	23.4	30.2	8.0	1.6	1.0	A-B-C
m-Xylene	—						C-A-B
m-Dichlorobenzene	—						C-A-B
Resorcinol	Acetone		36	8.5	2	1	C-A-B
m-Phenylenediamine	Acetone	4.8	45.2	8.4	2	1	C-B-A

TABLE V. CHEMICAL SHIFT IN *p*-di-X BENZENES

Compound	Solvent	$\tilde{\sigma}_B$ (in p.p.m.)
p-Dinitrobenzene	Acetone	−1.17
Terephthalaldehyde	Acetone	−0.77
p-Xylene	—	+0.29
p-Dichlorobenzene	Acetone	−0.05
p-Dibromobenzene	Acetone	+0.30
p-Phenylenediamine	Acetone	+0.85

TABLE VI. CHEMICAL SHIFT AND COUPLING CONSTANT IN *p*-XY BENZENES (in cps at 56.4 Mc)

Compound	Solvent	$\nu_0\tilde{\sigma}_{AB}$	J_{AB}	$\tilde{\sigma}_B$ (in p.p.m.)
p-Nitrobenzaldehyde	Acetone	12.3	9.3	−0.87
p-Nitrobenzoic acid	Acetone	23.1	8.4	
p-Nitrotoluene	—	38.1	9.5	−0.32
p-Nitrochlorobenzene	Acetone	31.7	9.0	−0.53
p-Nitrobromobenzene	Acetone	22.1	9.8	−0.71
p-Nitrophenol	Acetone	68.0	9.5	−0.23
p-Nitroaniline	Acetone	64.7	8.9	−0.05
p-Hydroxybenzaldehyde	Ethanol	46.7	9.5	
p-Aminobenzaldehyde	Acetone	45.8	8.2	+0.02
p-Toluic acid	Acetone	37.0	8.1	
p-Chlorotoluene	—	12.1	8.3	+0.27
p-Bromotoluene	—	22.9	8.2	+0.22
p-Cresol	—	0.0		
p-Toluidine	Ether	23.7	9.0	+0.69
p-Bromochlorobenzene	Acetone	11.6	8.8	
p-Chlorophenol	—	14.1		
p-Chloroaniline	Acetone	26.1	9.0	+0.51
p-Bromophenol	Ether	31.4	9.7	
p-Iodoaniline	Acetone	48.4	8.8	+0.41

while the C proton is not so much influenced.

The analyzed results are tabulated in Table IV. The perturbation treatment of the second order could be applied to two compounds (*m*-dinitrobenzene and *m*-dichlorobenzene) well, but not to the others where the resonance positions of A and B protons are closely located. For these compounds, the analysis of the spectrum should be accomplished with the higher order approximation.

p-Di-X Benzene.—The spectra are single line as expected from the symmetry consideration of this system. The chemical shift referred to benzene is shown in Table V.

p-XY Benzene.—This system has two different substituents and the different electronic effect is given on the proton neighboring to each of them. In addition to this, the spectrum of this system is comparatively simple and can be analyzed easily Therefore, the investigation of the spectrum of this system is interesting to show the overlapping extent of the effects of both substituents on the ring. An example of the spectrum of this system is shown in Fig. 1d. This consists of two groups A and B, which correspond to the protons A and B in the molecule.

This system has been analyzed for several compounds with appropriate approximation by Richards and Schaefer[7]. The present spectra were analyzed according to their method. The values of the chemical shift and the coupling constant obtained are listed in Table VI, where the J_{AB} is the coupling constant between A and B protons when the $J_{AB'}$ (coupling constant between A and B′ protons which one *p*-position to each other) is neglected.

Qualitatively, the shift between the two groups A and B is large when the electronic effects of the two substituents X and Y upon the ring protons are greatly different and vice versa. For example, $\tilde{\sigma}_{AB}$ of *p*-nitroaniline is very large where the electronic nature of NO_2 and NH_2 group are greatly different to each other as is well known by the evidence of their effect on the substitution reaction of ring protons, whereas the one of bromochloro-benzene is very small as is expected.

Other Systems.—The spectral figures of the other systems are generally more complicated than the systems described above. *o*-XY- and *m*-XY-benzenes are of this sort. These systems have no symmetry, therefore their analyses are of course very cumbersome. These systems will not be dealt with further in this paper.

The values of the coupling constant between two protons on the benzene ring are approximately definite with respect to their mutual *o*-, *m*- or *p*-positions. The values deduced from the results of the analyses may be summarized as follows;

J between two protons located at

o-position mutually	7∼9 cps
m-position mutually	1∼3 cps
p-position mutually	0∼1 cps

The values indicated that the coupling is attenuated in proportion to the exponent of about −5 to the direct bond length between the two protons concerned. The values listed above

coincide well with the description which appeared in the book of Pople et al.[8]

The resonance position of a benzene ring proton is closely related to the relative location of the proton to the substituent on the benzene ring. The same evidence was discussed by Gutowsky et al.[1] with the fluorobenzene derivatives. They showed also that the shift values for the ring fluorine of polysubstituted fluorobenzenes may be calculated from the shift values of monosubstituted fluorobenzenes with the assumption of an additive law of shift. Their calculated results with this law coincide with the experimental values with deviations less than 10%. We applied the law to the samples investigated. The values for the disubstituted benzenes were calculated with the shift values of the monosubstituted benzenes reported by Corio and Dailey[3]. The results of the calculation showed that the shift values do not necessarily coincide well, but showed a close relation with the experimental values. The explanation of the shift values with the additive law may of course be oversimplified by neglecting to take into account all the interactions in the molecule, and further consideration of the results will be postponed until more experimental data with monosubstituted benzenes become available.

The resonance lines for the protons just adjacent to the methyl group on the ring generally show fine structure. This splitting is illustrated in Fig. 1d for the ring proton resonance of *p*-toluidine. Hoffman[9] reported that the ring proton resonance line of mesitylene showed broadening, and he assumed that this broadening arose from the coupling between the ring proton and the methyl protons by hyperconjugation mechanism. Although the observed fine structure reported here may be a similar one to the case of mesitylene, further experimental verification seems necessary for deciding the true origin of the splitting.

The present work is carried out with saturated acetone solutions in almost all cases, however ; the solvent effect on the shift between ring protons appears to be noticeable. Thus the shift values may differ from one another among solutions with different concentrations. This intramolecular shift may be assumed to arise from the selective interaction between the proton located at the specific position on the ring and the solvent molecule. The nature of this interaction is at present unexplained.

8) Ref. 6, p 193, Table 8-1.
9) R. A. Hoffman, *Mol. Phys.*, **1**, 326 (1958).

Summary

High resolution proton magnetic resonance spectra of a variety of mono- and di-substituted benzenes were observed at 56.4 Mc. The spectra of molecules with higher symmetry were analyzed, and the values of chemical shifts among the ring protons and those referred to benzene were obtained as well as spin coupling constants. The spectra were discussed with correlation to the substituents.

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The Effect of Chain Branching and Molecular Weight of Polyethylene on its Glass Transition Temperature

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In the previous paper[1] the effects of chain branching, mainly short chain branching, on such properties as the melting point, the crystallizing temperature and the premelting phenomenon were reported and discussed. In this paper the effect of chain branching on the glass transition temperature and the degree of cubic expansion above and below the glass transition temperature are described.

Regarding the glass transition temperature, a sort of second-order transition temperature, of polyethylene, a number of reports have been presented. Hunter and Oakes[2] showed from the measurement of linear expansion that there was a sign of transition occurring at about $-45°C$. Later Danusso et al.[3] reported from the volume expansion measurement that the second-order transition temperature of polyethylene existed arround $-20°C$ regardless of molecular weight, degree of chain branching or degree of crystallinity. According to the paper of Gubler and Kovacs[4] the cubic expansion coefficient changes between -20 and $-25°C$ for both a high-pressure and a Ziegler polyethylene. It has also been confirmed by some other methods that a transition occurs at about $-20°C$ or at a still lower temperature[5-10]. By considering the change of mechanical properties of polyethylene at about $-50°C$, reported by Carey et al.[11], and the brittle point of $-68°C$ reported by Boyer and Spencer[12], this second-order transition at arround $-20°C$ seems to be the glass transition, though the existence of another transition at the temperature below $-100°C$ was reported by Schmieder and Wolf[13], Oakes and Robinson[14] and Dannis[15]. As for the effect of the degree of chain branchig on the glass transition temperature, it may be inferred from the results reported hitherto that the degree of chain branching has no effect on the glass transition temperature. Such a conclusion, however, can not be reached so hastily, as only a few kinds of samples were used in each experiment.

The glass transition temperature is generally defined as the point at which the main chain in an amorphous region of a polymer acquires large scale mobility. It is therefore expected that short chain branching and the branch point of long chain branching, which are contained in the amorphous region, disturb the regularity of molecules and keep the molecules from arranging themselves in good order in proportion to the number of them, and consequently the molecular mobility of the amorphous region is affected not a little by them; that is, the more branches the amorphous region contains, the more easily it initiates the large scale molecular motion and as a result the glass transition of polyethylene having the higher degree of chain branching occurs at the lower temperature.

From this point of view, a series of measurements have been taken by using various polyethylenes. From the results obtained it appears that short chain branching has a large effect on the glass transition temperature, independent of the degree of crystallinity. Long chain branching scarcely exists in low-pressure polyethylene, and in high-pressure polyethylene only a few long chain branching are contained in comparison with short one. It is therefore considered that its effect is not noticeable, even if each branch point has some effect on the glass transition temperature.

1) K. Tanaka, This Bulletin, **33**, 1060 (1960).
2) E. Hunter and W. G. Oakes, *Trans. Faraday Soc.*, **41**, 49 (1945).
3) F. Danusso, G. Moraglio and G. Talamini, *J. Polymer Sci.*, **21**, 139 (1956).
4) M. G. Gubler and A. J. Kovacs, *J. Polymer Sci.*, **34**, 551 (1959).
5) E. Butta and A. Charlesby, *J. Polymer Sci.*, **33**, 119 (1958).
6) C. W. Deeley, D. E. Kline, J. A. Sauer and A. E. Woodward, *J. Polymer Sci.*, **28**, 109 (1958).
7) N. Fuschillo, E. Rhian and J. A. Sauer, *J. Polymer Sci.*, **25**, 381 (1957).
8) A. H. Willbourn, *Trans. Faraday Soc.*, **54**, 717 (1958).
9) W. P. Slichter and D. W. McCall, *J. Polymer Sci.*, **25**, 230 (1957); **26**, 171 (1957).
10) P. W. Jensen, *J. Polymer Sci.*, **28**, 635 (1958).
11) R. H. Carey, E. F. Schultz and G. J. Dienes, *Ind. Eng. Chem.*, **42**, 842 (1950).
12) R. F. Boyer and R. S. Spencer, *J. Appl. Phys.*, **15**, 398 (1944).
13) K. Schmieder and K. Wolf, *Kolloid-Z.*, **134**, Sonderausgabe 2, Marburger Diskussionstagung: Das Relaxationsverhalten der Materie, 157 (1953).
14) W. G. Oakes and B. W. Robinson, *J. Polymer Sci.*, **14**, 505 (1954).
15) M. L. Dannis, *J. Appl. Polymer Sci.*, **1**, 121 (1959).

Samples

Samples used were Marlex 50-9, Ziegler polyethylene, and eight kinds of high-pressure polyethylenes with the different molecular parameters which were provided by courtesy of Dr. Hammer of E. I. du Pont de Nemours and Company. The molecular parameters are shown in Table I. Marlex 50-9 and Ziegler polyethylene were commercially available polymers made by Phillips Petroleum Company and Dow Chemical Company, respectively. As the molecular parameters for these two samples were not available, the degree of short chain branching was determined by the infra-red method according to Slowinski[16]. It was found to be 0.25 for Marlex 50-9 and 0.4 for Ziegler polyethylene.

TABLE I. THE MOLECULAR PARAMETERS FOR POLYETHYLENE SAMPLES

Sample	Melt index	$M_n \times 10^{-3}$	N_c*	N_w**
A***	0.2	34	1.6	20
B	2.1	32	1.6	18
C	2.1	21	2.2	27
D	2.1	18	3.0	34
E	3.8	20	1.6	13
F	2.0	50	2.0	18
G	1.8	27	0.6	10
H	16.0	12	3.2	29
Marlex 50-9			0.25	
Ziegler			0.4	

* Short chain branching index in CH_3 groups per 100 CH_2 groups.
** Long chain weight average number of branch points per molecule.
*** These (A to H) are high-pressure samples.

Experimental

Dilatometric measurements were at first taken in the temperature range from −40 to 150°C by using mercury as the confining liquid. However, it seemed to be undesirable to determine the glass transition point merely from the measurements in which mercury was used as the confining liquid, as the temperature range below the glass transition temperature was small. Therefore 99.5% ethanol being used as the confining liquid, measurements were carried out over the temperature range from room temperature to −70°C. In this measurement Bekkedahl's straight type dilatometer[17] was used and the preparation of the most highly crystallized sample was performed by following the way mentioned in the previous paper in the sufficiently evaluated glass tube in order to protect the sample from oxidation before it was enclosed in the dilatometer. A Dewar vessel containing toluene was used as a bath. The details about the experimental procedure were omitted in this paper, as they were described in the previous paper.

The glass transition temperature, T_g, was determined by extrapolation of two straight lines connected by a curved section, consisting of the volume-temperature curve of high polymer. As polyethylene is a semi-crystalline polymer and the difference between cubic expansion coefficients above and below T_g is small, an error is apt to be made. In order to eliminate such an error T_g was also determined from the discontinuity of the curve obtained by plotting the volume temperature derivatives, $\Delta V/\Delta t$, as a function of temperature as was done by Hoffmann and Weeks[18].

Results and Discussion

The specific volume-temperature curves of the most highly crystallized polyethylenes ranging from above to below the glass transition temperature are shown in Fig. 1. The volume temperature derivatives are plotted as a function of temperature in Fig. 2. In these two figures only a few curves were shown to avoid confusion.

The average value of the glass transition temperature obtained for each sample is given in Table II. These values are plotted in Fig. 3 as a function of the degree of short chain branching. As is shown in the figure, the glass transition temperature lowered with the increasing amount of short chain branching

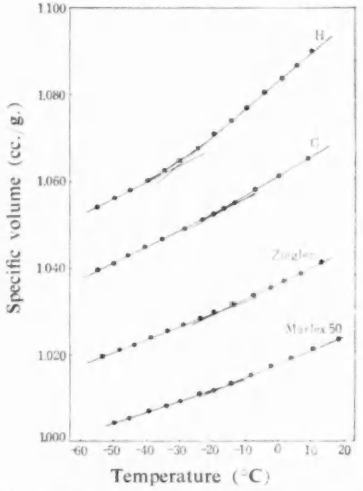

Fig. 1. Specific volume-temperature curves of the most highly crystallized polyethylene ranging from above to below T_g.

16) E. J. Slowinski, Jr., H. Walter and R. L. Miller, *J. Polymer Sci.*, **19**, 353 (1956).
17) N. Bekkedahl, *J. Research Natl. Bur. Standards*, **42**, 145 (1949).
18) J. D. Hoffmann and J. J. Weeks, *J. Research Natl. Bur. Standards*, **61**, 465 (1958).

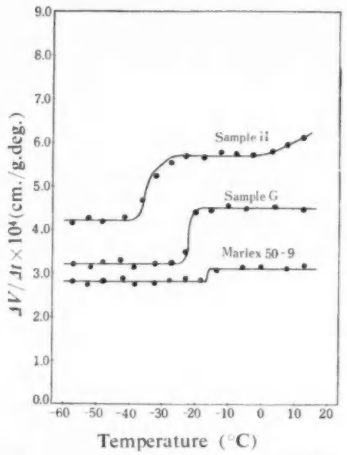

Fig. 2. Volume-temperature derivatives of some of the most highly crystallized samples as a function of temperature.

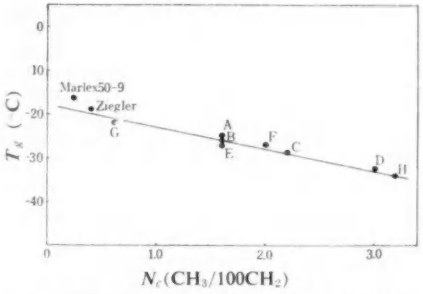

Fig. 3. T_g as a function of degree of short chain branching

and there seems to be a linear relation between the glass transition temperature and the degree of short chain branching.

The degree of cubic expansion above and below the glass transition temperature, which are presented by the gradients of the straight lines above and below the temperature, are also listed in Table II. These values generally increased as the amount of short chain branching became larger and those above the glass transition point increased in a greater extent than did those below the point, which fact is probably because the large-scale segmental motion in the amorphous region is excited at the temperature above the glass transition point and the more the sample of polyethylene branched, the greater is the scale of the motion. As regards the degree of cubic expansion below the glass transition point there is a view by Price[19] and Danusso et al.[20]

Table II. The glass transition temperatures and degrees of cubic expansion above and below that temperature

Sample	N_c	T_g	$\alpha_1^* \times 10^4$	$\alpha_2^{**} \times 10^4$
Marlex 50-9	0.25	−16.0	2.8	3.1
Ziegler	0.4	−19.1	2.8	3.4
G	0.6	−22.2	3.2	4.5
A	1.6	−25.2	3.9	5.1
B	1.6	−25.8	3.5	5.0
E	1.6	−26.3	3.7	5.3
F	2.0	−27.3	4.0	5.3
C	2.2	−28.8	3.9	5.2
D	3.0	−32.5	4.1	5.9
H	3.2	−34.0	4.2	5.7

* Degree of expansion below T_g.
** Degree of expansion above T_g.

that it is considered to be equal for all the polyethylene, but in this experiment the result as above was obtained, that is, the degree of cubic expansion below the glass transition point increased as a whole with the increase of the degree of short chain branching.

Since short chain branching affects the degree of crystallinity of polyethylene as was mentioned in the previous paper, it is expected that the lowering of the transition temperature by the increase of short chain branching shown in Fig. 3 is attributable to the decrease of the degree of crystallinity. However, glass transition temperatures of the quenched samples of these polyethylenes, which showed a low degree of crystallinity about 40% at 25°C, were found at nearly equal temperatures to those of crystallized samples. Therefore the lowering of the glass transition temperature is probably due to the direct effect of short chain branching itself and not to the decrease of the degree of crystallinity. According to the recent result of linear expansion measurements by Saito[21], a transition was found at around −32°C for a low-branched polyethylene and at about −45°C for a highly-branched polyethylene. The difference between these temperatures was almost equal to that found by the author, though each temperature was lower by about 10 degrees than that obtained here.

Considering the results mentioned above, short chain branching of polyethylene appears to affect the glass transition temperature independent of such factors as degree of crystallinity and molecular weight. Moreover, according to Gubler and Kovacs[1] the number of CH_2 groups constituting the main chain in amorphous regions of polyethylene thermally

19) F. P. Price, *J. Chem. Phys.*, **19**, 973 (1951).
20) F. Danusso, G. Moraglio and G. Natta, *Ind. Plastiques Mod. (Paris)*, **10**, 40 (1958).
21) S. Saito, private communication.

treated in the same way are almost equal regardless of its kind. Therefore the polyethylene having the higher degree of short chain branching will contain more branches in one amorphous region, provided that short chain branching is distributed equally in all the amorphous regions. It is considered that the shorter the branches which are contained in the amorphous regions equal in size, the smaller is the intermolecular interaction between the segments in those regions in the temperature range below the glass transition temperature, and as a result the Macro-Brownian motion in amorphous regions starts at the lower temperature, that is, the glass transition occurs at the lower temperature.

The relation between the glass transition temperature and degree of short chain branching in high pressure polyethylene shown in Fig. 3 is led to the following expression by using the method of least square,

$$T_g = -4.6N_c - 18.7$$

Marlex 50-9 and Ziegler polyethylene deviate somewhat from this expression. According to Willbourn[22] short chain branches of high-pressure polyethylene are ethyl and butyl branches and those of Marlex and Ziegler polyethylene are methyl, and methyl and ethyl, respectively. Therefore in the amorphous region of Marlex 50-9 and Ziegler polyethylene molecules possess a greater intermolecular interaction than expected from the case of high-pressure polyethylene.

As in short chain branching, so in long chain branching, it is expected that the increasing amount of long chain branching lowers the glass transition temperature. In this experiment, however, no appreciable result was produced. This is probably attributable to the very small amount of long chain branching, that is, the effect of long chain branching on the glass transition temperature is covered by the effect of short chain branching and of molecular weight. For example, as to the samples A, B and E which were equal in degree of short chain branching but different in degree of long chain branching, even the reverse phenomenon was observed that the sample having the larger amount of long chain branching showed a higher glass transition temperature. It is perhaps due to the effect of molecular weight of the sample as is discussed below.

It is generally said that the glass transition temperature is affected by molecular weight. Molecular weights of the samples used cover a wide range, so transition temperaturs are illustrated in Fig. 4 as a function of molecular weight. In the figure the glass transition temperature apparently rises with the increase of molecular weight, but short chain branching considerably affects the glass transition temperature as was stated above. A definite conclusion cannot be deduced without eliminating the effect of short chain branching. In order to remove this effect, the difference between the glass transition temperature obtained from practical measurement and that from the expression already presented is illustrated in Fig. 5 as a function of molecular weight. As is shown in the figure the rise of the glass transition temperature is only less than 2°C as molecular weights increase from 10,000 to 50,000. Therefore it will be evident that molecular weight has a smaller effect on this transition temperature compared with that of short chain branching. According to Fox and Flory[23], however, the glass transition temperature of atactic polystyrene rose by 14°C as the molecular weight increases from 10,000 to 50,000 as is shown in Fig. 5. This difference in polyethylene and polystyrene is probably due to the fact that the former is a crystalline polymer and the latter an amorphous polymer,

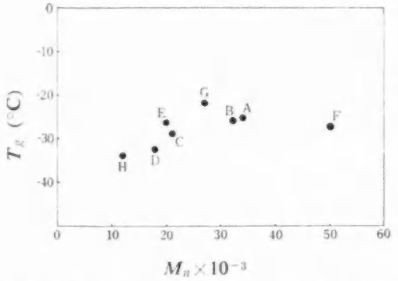

Fig. 4. T_g as a function of molecular weight.

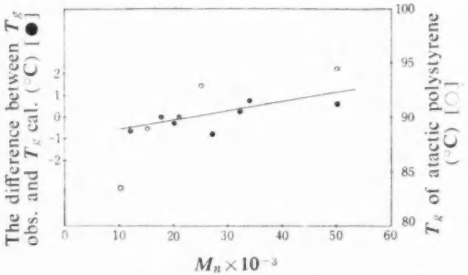

Fig. 5. The difference between T_g from the practical measurement and that from the expression presented in this paper, and T_g of atactic polystyrene are illustrated as a function of molecular weight.

22) A. H. Willbourn, *J. Polymer Sci.*, **34**, 569 (1959).

23) T. G. Fox, Jr. and P. J. Flory, *J. Appl. Phys.*, **21**, 581 (1950).

that is, this contains very large amorphous regions, whose size is greatly affected by molecular weight, while that includes alternately crystalline and amorphous regions. According to Gubler and Kovacs the size of the individual amorphous region in the samples thermally treated in the same way is almost equal regardless of the kind of polyethylene, as was mentioned already. From this point of view, it is considered that the effect of molecular weight on the glass transition temperature is essentially very small in polyethylene.

In addition it is reported by Smith[24] that polyethylene contains double bonds in it and most of them belong to the terminal of the main chain for Marlex and to the side chain for high-pressure polyethylene. But, as the amount of double bonds is very small, the effect on the glass transition temperature and degree of crystallinity will not be worth discussing in this paper.

Summary

A series of measurements by volume dilatometry were performed in order to know whether short chain and long chain branchings, and molecular weight of polyethylene affected the glass transition temperature or not. The glass transition temperature, T_g, was obtained from the intersection of two straight lines of volume-temperature curve and from the discontinuity of the curve obtained by plotting the volume temperature derivatives as a function of temperature. T_g lowered with the increasing amount of short chain branching and there seems to be a linear relationship between T_g and the degree of short chain branching. No appreciable effect of long chain branching on T_g was observed. T_g rose apparently with the increase of molecular weight, but the true rise of T_g was only less than 2°C as molecular weight increased from 10,000 to 50,000. The degree of cubic expansion above and below T_g increased generally as the amount of short chain branching increased.

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24) D. C. Smith, *Ind. Eng. Chem.*, **48**, 1161 (1956).

On the Thermal Dissociation of Organic Compounds[1]. *XIV. The Effects of the Solvents and of the Substituents on the Thermal Dissociation of Urethans in Amines*

By Teruaki MUKAIYAMA, Toyohiko AKIBA and Tamio ASAHI

(Received February 17, 1960)

In previous papers[2,3] of this series the kinetic studies of the dissociation of *N*-phenyl-alkyl carbamates in basic solvents were described. *N*-phenyl-alkyl carbamates dissociate in the presence of 10 molar excess of an amine at above 120°C; however, *N*-phenyl-phenyl carbamates dissociate instantly under the same condition.

In the case of *N*-phenyl-phenyl carbamates, the addition reaction of isocyanates with phenols to form urethans, which is the reversal of the dissociations, reaction do not proceed under the experimental conditions. Therefore, the dissociation proceeds to essentially 100% completion in the presence of an equimolar amount of an amine.

$$RHNCOOR \rightleftarrows R\text{-}N{=}C{=}O + HO\text{-}R \quad (1)$$

$$R\text{-}N{=}C{=}O + HNR'R' \rightleftarrows RHNCONR'R' \quad (2)$$

As described in the previous papers, reaction 1 is the rate-determining step in the above

1) This investigation was performed at the Gakushuin University.
2) T. Mukaiyama and Y. Hoshino, *J. Am. Chem. Soc.*, **78**, 1946 (1956).
3) T. Mukaiyama and M. Iwanami, ibid., **79**, 73 (1957).

sequence and the rate constants for the dissociation of urethans can be measured by determining the amount of the remaining amine.

The kinetic order of the dissociation of urethans was studied by the effect of change of initial concentration of both urethan and amine and it was shown that the dissociation is of the first order with respect to urethan and to amine respectively.

In order to study the effects of amines and solvents on the rate of dissociation of urethans, eight amines such as di-*n*-butyl amine and benzyl amine and ten inert solvents such as nitrobenzene and cumene were used. It was observed that the rates of the dissociation increased as the base strength of amines increased and the rates increased also as the dielectric properties of solvents increased.

The rates of dissociation of *N*-phenyl-phenyl carbamates substituted with methyl, methoxyl, chloro and nitro groups in the ortho, meta and para positions were determined to clarify the effects of substituents on the dissociation of urethans in amines. The results show that meta and para substituted *N*-phenyl-tolyl carbamates, N-phenyl-anisyl carbamates and unsubstituted urethans follow the Hammett equation with a positive ρ value, but *N*-phenyl-chlorophenyl carbamates and *N*-phenyl-nitrophenyl carbamates dissociate rapidly and deviate from the linear relationship of the Hammett equation. Except in the case of the methyl derivative, ortho-substituted urethans dissociate faster than the corresponding meta and para substituted urethans; this may be attributed to steric effects.

It can be concluded that, in amine, the dissociation proceeds via the concerted mechanism involving both urethan and amine.

TABLE I. MELTING POINTS AND ANALYSES FOR $C_6H_5NHCOOC_6H_4R$

R	M. p. °C	Nitrogen, % Calcd.	Found
o-Methoxy	151～152 (136)[a]	5.71	5.94
m-Methoxy	119	5.71	5.93
p-Methoxy	133	5.71	5.83
o-Methyl	143 (144)[b]		
m-Methyl	123～123.5 (125)[b]		
p-Methyl	114～115 (115)[b]		
H	126 (124)[c]		
o-Chloro	122～122.5 (120～121)[d]		
m-Chloro	124～125	5.65	5.95
p-Chloro	140～141 (138)[e]		
m-Nitro	129～129.5 (129)[f]		
p-Nitro	145～146 (147～148)[g]		

a) A. Morel, *Bull. soc. chim. France*, (3) **21**, 827 (1899).
b) E. Fromm and H. Eckhard, *Ber.*, **56**, 953 (1923).
c) R. Leuckart, *J. prakt. Chem.*, (2) **41**, 318 (1890).
d) A. Michael and P. Cobb, *Ann.*, **363**, 92 (1908).
e) A. Hantzsch and L. Mai, *Ber.*, **28**, 979(1895).
f) O. Brady and J. Harris, *J. Chem. Soc.*, **127**, 2176 (1925).
g) M. Busch, G. Blume and E. Pungs, *J. prakt. Chem.*, [2] **79**, 534 (1909).

Experimental

Procedure. — The experimental procedure was essentially that used in the earlier investigation[2,3]. The amount of the amine remaining was determined by titrating with 0.025 N hydrochloric acid, using Bromocresol Green as indicator.

Materials. — N-phenyl-phenly carbamates were prepared from phenyl isocyanate and the purified corresponding phenols according to the procedure of Leuckart[4]. Amines and solvents were purified by distillation. The boiling points for these substances are listed in Table I and II.

TABLE II

Amines	B. p. °C/mmHg	Solvents	B. p. °C/mmHg
Di-benzyl	187/18	Anisole	153～154
Benzyl	89～90/12	Tetralin	92/18
Cyclohexyl	130.5～131	Decarlin	192
Di-isobutyl	139	Nitrobenzene	93/11
2-Ethylhexyl	165～165.5	Phenetole	167～168
Di-*n*-butyl	158～159	Triethyl-benzene	104～155/20
Lauryl	133～134/15	Cumene	150～151
n-Hexyl	129	Cymene	174～176
		o-Xylene	141.5～142
		p-Xylene	137.5

Results

The second order rate constant k_2 was calculated by Eq. 3

$$k_2 = 1/t \cdot x/a\ (a-x) \qquad (3)$$

where t, the time in second; x, the amount of reacted amine at time t; a, the initial concentration of both urethan and amine.

The values of the second order coefficient k_2 remained constant until the 60% of the dissociation with a tendency to drift upward in the later stage of the dissociation. It can be considered that the upward drift of k_2 might result from weak catalysis of the dissociation by urea or phenol produced. This was confirmed by the demonstration of the catalytic effect of added urea. The results are shown in Table III and Fig. 1. The addition of phenol to the reaction showed no effect on the rate of dissociation.

4) R. Leuckart, *J. prakt. Chem.*, [2] **41**, 318 (1890).

Table III. Catalytic effect of added 1-phenyl-3,3-dibenzylurea on the dissociation of *N*-phenyl-phenyl carbamate in benzyl amine, both 0.0535 mol./l. in nitrobenzene solvent at 94°C

Urethan mol.	Urea mol.	$k_2\times10^3$ l. mol^{-1} sec^{-1}
1	0	2.20
1	1	2.85
1	2	3.40

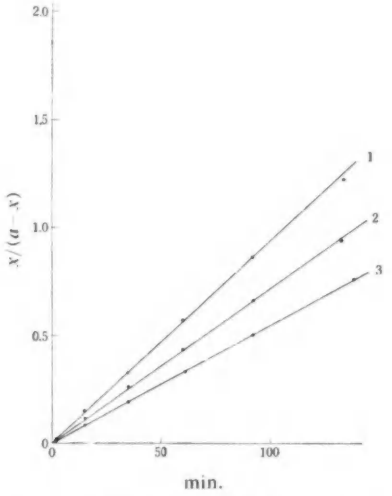


Fig. 1. Second-order plots of the thermal dissociation of *N*-phenyl-phenyl carbamate in benzyl amine and nitrobenzene in the presence or absence of 1-phenyl-3,3-dibenzylurea at 94°C.

	Urethan, mol.	Urea, mol.
1)	1	2
2)	1	1
3)	1	0

The kinetic order of the dissociation of urethans in amines were examined further by changing the initial concentration of both the urethan and the amine. The second order rate constants are nearly constant when the initial concentration of the reactants are changed from 1/2 : 1/2 to 2 : 2. When the molar ratio of the initial concentration of urethan to amine are changed from 1 : 1 to 1 : 10, the rates of dissociation increase as the amine concentration increases. When the molar ratio of urethan to amine is less than 2.5, the rate did not conform to the second order kinetics, but a first order plot fits the data well. The k_2 values calculated by dividing the k_1 value thus obtained by the concentration of the amine are nearly equal as shown in Table IV.

Table IV. Effect of variation of the relative concentration of *N*-phenyl-phenyl carbamate and di-*n*-butyl amine, both 0.0535 mol./l. in nitrobenzene solvent at 25°C and 45°C

Temp. °C	Urethan mol.	Amine mol.	$k_1\times10^6$ sec^{-1}	$k_2\times10^4$ l. mol^{-1} sec^{-1}
25	1	1		5.93
	2	2		6.80
	1	2.5	8.24	6.16
	1	5	16.3	6.09
	1	7.5	23.5	5.85
	1	10	27.4	5.12
45	1/2	1/2		31.2
	1	1		27.0
	2	2		35.6

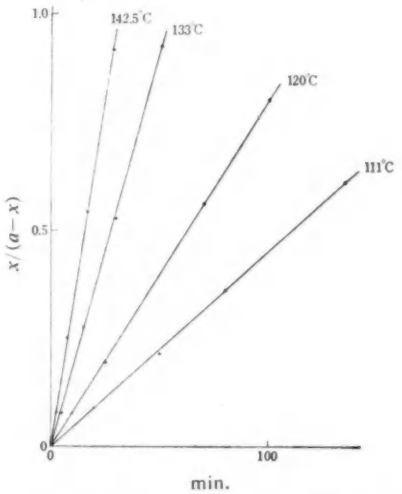


Fig. 2. Second-order plots of the thermal dissociation of N-phenyl-phenyl carbamate in dibenzyl amine and nitrobenzene.

The second order rate constants of various substituted urethans in amines and various inert solvents were obtained. As a typical run, the dissociation of *N*-phenyl-phenyl carbamate in dibenzyl amine and nitrobenzene at temperature betewen 111~142.5°C is shown in Fig. 2. The rate constants of the dissociation of *N*-phenyl-phenyl carbamates in amines were calculated by the method of least squares and are shown in Tables V—VII.

The plot of the logarithm of the rate constants vs. reciprocal absolute temperature gave satisfactory straight lines from which the activation energies and the entropies of activation were calculated by the method of least squares (Tables V—VII).

TABLE V. THE RATE CONSTANTS AND THE THERMODYNAMIC QUANTITIES FOR THE DISSOCIATION OF *N*-PHENYL-PHENYL CARBAMATE AND VARIOUS AMINES, BOTH 0.0535 mol./l. IN NITROBENZENE SOLVENT

Amines	Temp. °C	$k_2 \times 10^3$ l. mol^{-1} sec^{-1}	E kcal.	$\Delta S^{\neq}$ e. u.
Dibenzyl	111	1.45 ±0.01	21.0±0.2	−17.3±1.2
	120	2.52 ±0.02		
	133	5.89 ±0.09		
	142.5	11.2 ±0.03		
Benzyl	94	2.21 ±0.03	19.2±0.4	−18.6±2.5
	103	4.33 ±0.11		
	113	8.04 ±0.00		
	133	23.7 ±0.09		
n-Hexyl	61	2.83 ±0.07	13.8±0.08	−29.5±0.5
	70	5.08 ±0.01		
	80	8.61 ±0.05		
	89	14.3 ±0.13		
Cyclohexyl	61	1.99 ±0.04	15.3±0.45	−25.4±2.5
	70	3.53 ±0.01		
	80	6.28 ±0.06		
	89	12.1 ±0.09		
2-Ethylhexyl	61	1.37 ±0.03	15.2±0.16	−26.6±0.9
	70	2.28 ±0.02		
	80	4.30 ±0.06		
	89	7.36 ±0.09		
Di-isobutyl	61	1.05 ±0.00	15.6±0.33	−25.6±1.9
	70	2.06 ±0.00		
	80	4.04 ±0.02		
	89	6.86 ±0.05		
Lauryl	35	0.611±0.00	14.6±0.7	−26.2±4.0
	45	1.05 ±0.08		
	55	2.92 ±0.00		
	80	12.2 ±0.00		
Di-*n*-butyl	25	0.593±0.00	15.1±0.3	−20.6±1.4
	35	1.36 ±0.00		
	45	2.73 ±0.00		
	60	8.75 ±0.00		

Discussion

The rate constants of the dissociation of urethans in various amines increase in the following order,

di-*n*-butyl ≫ lauryl > *n*-hexyl,

cyclohexyl > 2-ethylhexyl,

di-isobutyl > benzyl ≫ dibenzyl.

As noted in the above sequence, urethans dissociate rapidly in di-*n*-butyl amine (K_b= 2.05×10^{-3}, at 25°C), moderately in cyclohexyl amine ($K_b=4.39\times10^{-4}$, at 25°C) and slowly in benzyl amine ($K_b=2.4\times10^{-5}$, at 25°C).

The activation energies of the dissociation of urethans in weak bases such as benzyl amine and dibenzyl amine are greater than those in strong bases such as di-*n*-butyl amine.

The results show that, in amines the rates of dissociation increase as the basicities of the amines increase and it can be concluded that the dissociation proceeds via the base catalyzed mechanism in which the process of deprotonation of urethans by a base is a predominant factor.

The rates of dissociation are also affected by the nature of inert solvents. The rate constant of dissociation in a polar solvent such as nitrobenzene is much larger than that in a non-polar solvent such as tetralin and *m*-xylene. As shown in the following sequence, the rates increase as the dielectric properties of solvent increase.

Nitrobenzene ≫ anisole, phenetole >

tetralin, decalin, *o*-xylene, cumene,

triethylbenzene, *m*-xylene, cymene

The results suggest an important solvent interaction in the dissociation process which may stabilize the forming phenoxyl ion and facilitate the cleavage of the carbon-oxygen bond in the activated state.

The results of the rate measurement given in Table VII show that for substitution in the *meta* and *para* position, the greater the electron-attracting power of the substituents, the greater

TABLE VI. THE RATE CONSTANTS AND THE THERMODYNAMIC QUANTITIES FOR THE DISSOCIATION OF *N*-PHENYL-PHENYL CARBAMATE AND DI-*n*-BUTYL AMINE, BOTH 0.0535 mol./l. IN VARIOUS SOLVENTS

Solvent	Temp. °C	$k_2 \times 10^3$ l. mol^{-1} sec^{-1}	E kcal.	$\Delta S^{\neq}$ e. u.
Decalin	70	0.767±0.06	14.6±0.5	−30.5±2.61
	80	1.30 ±0.01		
	90	1.86 ±0.02		
	100	4.24 ±0.01		
Tetralin	70	0.900±0.00	15.2±0.1	−28.5±0.53
	80	1.67 ±0.01		
	90	3.06 ±0.76		
	100	5.85 ±0.03		
Anisole	70	1.96 ±0.01	15.0±0.5	−27.6±2.95
	80	3.27 ±0.00		
	90	6.01 ±0.00		
	100	11.4 ±0.27		
Nitrobenzene	25	0.593±0.00	15.1±0.25	−20.6±1.4
	45	1.36 ±0.00		
	60	2.73 ±0.00		
	80	8.75 ±0.00		
Cumene	80	1.31 ±0.06	17.4±1.6	−22.6±8.8
	90	2.61 ±0.01		
	100	5.09 ±0.00		
	110	8.88 ±0.24		
Cymene	80	1.01 ±0.01	17.3±0.3	−23.5±1.0
	90	2.03 ±0.00		
	100	3.93 ±0.06		
	110	7.09 ±0.02		
Phenetole	80	2.09 ±0.00	19.0±0.2	−17.3±1.1
	90	4.28 ±0.02		
	100	9.45 ±0.12		
	110	17.3 ±0.27		
Triethylbenzene	80	1.24 ±0.02	17.1±0.1	−23.7±0.3
	90	2.45 ±0.02		
	100	4.60 ±0.16		
	110	8.42 ±0.19		
o-Xylene	80	1.34 ±0.01	16.7±0.3	−24.7±0.5
	90	2.62 ±0.04		
	100	4.81 ±0.07		
	110	8.36 ±0.12		
m-Xylene	80	1.13 ±0.01	17.2±0.7	−23.6±1.9
	90	2.17 ±0.02		
	110	7.71 ±0.07		

are the rate constants and the lower the activation energy; the greater the electron-donating power of the substituents, the lower are the rate constants and the greater the activation energy. The logarithm of the k of the dissociation of methyl and methoxy substituted urethans and unsubstituted urethan is a linear function of the substituent constants given by Hammett and the gradient of the plot gave values for the reaction constant, ρ, of 1.72 in di-*n*-butyl amine and of 1.90 in benzyl amine, respectively. *N*-phenyl-chlorophenyl carbamate and *N*-phenyl-nitrophenyl carbamate dissociate very rapidly and deviate from the linear relationship of the Hammett equation.

The rates of dissociation of various substituted urethans in di-*n*-butyl amine are greater than those in benzyl amine and the activation energies and the entropies of activation in di-*n*-butyl amine are lower than those in benzyl amine. As mentioned above, the rates of dissociation depend on the basic strength of amine and the results might be attributed to the basicity of the amines which participate in the deprotonation of urethans in the dissociation process.

The higher rates with lower activation energies for the dissociation of urethans with electron-attracting substituents such as chloro and nitro groups may be ascribed to the stability of the phenoxyl ion dissociated. The phenoxyl ion with electron-attracting groups is

TABLE VII. THE RATE CONSTANTS AND THE THERMODYNAMIC QUANTITIES FOR THE DISSOCIATION OF *N*-PHENYL-PHENYL CARBAMATES AND AMINES, BOTH 0.044 mol./l. IN NITROBENZENE SOLVENT

a) In di-*n*-butyl amine:

Substituents	Temp. °C	$k_2 \times 10^3$ l. mol^{-1} sec^{-1}	E kcal.	ΔS^* e. u.
o-Methyl	60	1.50 ±0.13	16.6±0.4	−21.5±2.7
	70	3.48 ±0.18		
	80	6.26 ±0.21		
	90	12.2 ±0.53		
m-Methyl	50	2.07 ±0.20	16.4±0.3	−20.2±1.8
	60	3.48 ±0.17		
	70	8.07 ±0.24		
	80	17.7 ±0.00		
p-Methyl	60	2.64 ±0.01	16.2±0.1	−23.2±0.4
	70	6.42 ±0.13		
	80	10.6 ±0.29		
	90	20.1 ±0.92		
o-Methoxy	40	5.27 ±0.14	13.1±0.2	−21.1±1.1
	50	10.64 ±0.00		
	60	19.3 ±0.51		
m-Methoxy	70	1.95 ±0.20	15.8±0.2	−20.3±1.4
	80	4.1 ±0.96		
	90	6.76 ±0.43		
	100	12.4 ±0.12		
p-Methoxy	60	1.90 ±0.00	14.5±0.0	−27.4±0.2
	70	3.60 ±0.15		
	80	7.51 ±0.26		
	90	11.65 ±0.28		
o-Chloro	0	3.62 ±0.27	11.6±0.0	−26.4±0.1
	15	17.8 ±1.3		
	25	36.1 ±0.0		
	35	66.0 ±0.22		
m-Chloro	0	1.47 ±0.02	12.4±0.3	−26.1±1.6
	15	4.50 ±0.82		
	25	12.8 ±0.82		
	35	19.6 ±0.02		
p-Chloro	0	0.455±0.01	13.3±0.2	−25.2±1.4
	15	1.02 ±0.08		
	25	3.37 ±0.00		
	35	7.45 ±0.07		
m-Nitro		fast		
p-Nitro		very fast		

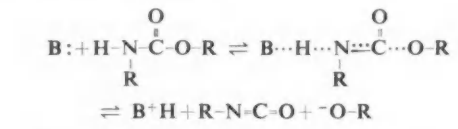
b) In benzylamine:

o-Methyl	110	2.40 ±0.32	21.4±0.91	−15.4±4.5
	120	5.10 ±0.14		
	140	21.5 ±1.03		
m-Methyl	110	4.33 ±0.03	17.1±0.3	−25.3±1.6
	120	7.97 ±0.02		
	130	12.9 ±0.00		
	140	22.7 ±0.01		
p-Methyl	110	2.56 ±0.01	17.7±0.6	−24.7±0.0
	120	4.20 ±0.02		
	130	8.39 ±0.00		
	140	13.2 ±0.02		
o-Methoxy	100	8.70 ±0.06	19.1±1.4	−15.5±7.2
	110	14.9 ±0.71		
	120	37.5 ±0.85		
	130	55.2 ±0.50		

TABLE VII (continued)

Substituents	Temp. °C	$k_2 \times 10^3$ l. mol^{-1} sec^{-1}	E kcal.	ΔS^* e. u.
m-Methoxy	100	7.3 ±0.64	16.8±0.5	−24.2±2.3
	110	11.0 ±0.29		
	120	18.5 ±0.65		
p-Methoxy	110	2.72 ±0.17	20.7±0.7	−16.8±3.8
	120	4.73 ±0.36		
	130	9.60 ±0.28		
o-Chloro	50	5.43 ±0.07	14.0±1.3	−24.7±6.7
	60	12.7 ±0.41		
	70	21.8 ±1.31		
	80	49.8 ±0.98		
m-Chloro	60	7.67 ±0.00	15.3±0.0	−22.6±0.2
	70	15.2 ±0.00		
	80	28.5 ±0.03		
	90	71.9 ±1.11		

more stable than that with electron-donating groups and this ion stabilizing effect may be the chemical driving force in the following dissociation mechanism.



The above one step mechanism involving urethan and amine can be confirmed by the rate dependency on both factors. In the strong bases, such as aliphatic amines, the dissociation proceeds by bimolecular concerted mechanism and not by termolecular mechanism as proposed in the previous reports[2,3].

Summary

N-phenyl-phenyl carbamates dissociate into their component compounds very readily in the presence of a base. Unlike the case of *N*-phenyl-alkyl carbamates, *N*-phenyl-phenyl carbamates dissociate in the presence of an equimolar amount of an amine at lower temperature. The kinetics of the dissociation of *N*-phenyl-phenyl carbamates were of the first order with respect to carbamates and of the first order with respect to base.

The rate constants, the activation energies and the entropies of activation of the dissociation of *N*-phenyl-phenyl carbamates in various amines and solvents were measured throughout temperature interval 0～140°C.

The effects of amines, solvents and substituents on the dissociation of urethans in amines were studied.

The authors wish to express their hearty thanks to Professor Toshio Hoshino for his encouragement throughout the course of this experiment.

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Rates of Solvolysis of 2-Hydroxycyclohexyl Brosylates

By Nobuo Mori

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In the present paper there will be reported the preparation and the solvolysis rates of *cis*- and *trans*-2-hydroxycyclohexyl brosylates. The *cis* isomer used for solvolysis is a new substance and could not be prepared by the usual method[1]. The *cis* isomer has now been obtained in a good yield by the reaction of *cis*-cyclohexane-1, 2-diol with 2 to 3 equivalent quantities of *p*-bromobenzenesulfonyl chloride in dry pyridine.

The solvolysis rates were measured at 99.8°C in ethanol (98.5% by weight) and also in acetic acid containing a slight excess of acetic anhydride. In all cases, the observed rates, especially in ethanol, were of the first order and the error of the measurements was always lower than 5%. In acetolysis, one free hydroxyl group in each of the isomers will react with acetic acid to form 2-acetoxycyclohexyl brosylate, especially in the presence of *p*-bromobenzenesulfonic acid liberated during the solvolysis. Therefore, a calculated first order rate constant in a run in acetic acid will change continuously and gradually. However, the rates were nearly of the first order. Table I lists the data for a run with *trans*-2-hydroxycyclohexyl brosylate in acetic acid. It is seen that in the run the first order rate constant is almost constant. The slight increase of the rate the during run is probably attributed to the accompanying acetolysis of the corresponding acetoxy cyclohexyl brosylate formed.

Table I. Acetolysis of *trans*-2-hydroxycyclohexyl brosylate in acetic acid at 99.8°C

Time (min.)	Brosylate (mol./l.)	$k_1 \times 10^5$ (min^{-1})
0.0	6.16×10^{-3}	
30	3.36	2.02
50	2.20	2.06
70	1.49	2.02
90	0.91	2.12
110	0.051	2.26
150	0.016	2.44
	Mean	2.15

The rate constants and the relative rates for the isomeric brosylates are summarized in Table II.

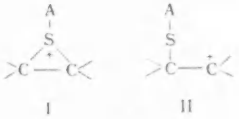
Table II. Rate constants and relative rates for brosylates at 99.8°C

2-Substituent	$k_1 \times 10^5$, min^{-1} EtOH	AcOH	k_{cis}/k_{trans} EtOH	AcOH
cis-OH	9.5	2.23	1.1	1.03
trans-OH	8.5	2.15		
cis-OAc		0.0058*		
trans-OAc		3.1*		
H		ca. 11**		

* From data in Ref. 1

** Calculated from data at lower temperatures in Ref. 1

Generally, in solvolysis of 2-functionally substituted cyclohexyl brosylates and tosylates, the reaction rate of the *trans*-forms is larger than that of the *cis*-form. For example, the relative rates of acetolysis (at 75°C) of 2-acetoxycyclohexyl *p*-brosylates are in the following sequence[1]: unsubstituted(1.0)>*trans* (0.3)≪*cis*(1.31×10^{-4}). In those cases, with the *trans*-group, the reaction proceeds substantially by way of cyclic ion I, and with the *cis*-group, probably carbonium ion II.



I II

However, unlike those compounds, the reactivity of *cis*-2-hydroxycyclohexyl brosylate is slightly greater than that of the *trans*-isomer. Further, the rate constants for the brosylates are in the same order as that for unsubstituted cyclohexyl *p*-brosylate (see Table II). The slightly higher reactivity of the *cis*-isomer and the very small difference in reactivity between the *cis*- and *trans*-isomers can not be explained on the basis of the participation of hydroxyl group alone. The high reactivity of the isomers is probably due to the participation of the hydrogen atom in β-position similar to unsubstituted cyclohexyl brosylate, rather than due to that of hydroxyl group. The fact that the reactivity of the *cis*-isomer is higher than that of the *trans*-isomer is mainly due to steric acceleration based on 1*a*, 3*a*-interaction (or B-strain). Those facts are in good agreement

1) S. Winstein, E. Grundwald and L. L. Ingraham, *J. Am. Chem. Soc.*, **70**, 821 (1948).

with the behavior in solvolysis of 2-*tert.*-butylcyclohexyl *p*-tosylate[2].

Experimental

Samples and Solvents. *cis*-2-Hydroxycyclohexyl *p*-Brosylate.—A solution of 0.5g. of *cis*-cyclohexane-1,2-diol (m. p. 97°C., prepared from cyclohexene in *tert.*-butanol with OsO_4[3]) in 2cc. of dry pyridine was treated with 2.5g. of *p*-bromobenzenesulfonyl chloride at 5 to 10°C. After 30 to 40 min. the mixture was diluted with cold 6N HCl and the oily product precipitated was triturated with dil. HCl repeatedly to solidify. After recrystallization from benzene and ligroin (b. p. 75~120°C), 0.7g. of the *cis*-brosylate was obtained as brittle needles, m. p. 110.6°C.

Found: C, 42.93; H, 4.80. Calcd. for $C_{12}H_{15}O_4SBr$: C, 42.99; H, 4.51%.

***trans*-2-Hydroxycyclohexyl *p*-Brosylate** was obtained with a good yield from *trans*-cyclohexane-1,2-diol (m. p. 102~104°C., prepared from cyclohexene and hydrogen peroxide in formic acid[4]) in an analogous way to the *cis*-isomer. After recrystallization from benzene and ligroin, the *trans*-brosylate was obtained as needles, m. p. 108°C (reported 106.9~108.8°C[2]).

Ethanol (98.5% by weight).—Commercial reagent grade absolute ethanol was fractionally distilled.

Acetic Acid.—Reagent grade glacial acetic acid was crystallized twice by the freezing method, refluxed with 2% by weight of acetic anhydride and 1% by weight of anhydrous sodium acetate for 3 hr., and distilled.

Procedure for Rate Measurements[5].—The sample was weighed out and made up to volume in the solvent at 15~20°C. About 6~7cc. portions were sealed in tubes and immersed in vapor over boiling water (99.8°C). Time was counted from immersion of the tube to its removal and quenching in ice-water. After being cooled the tube was allowed to come to room temperature and then opened, a 5cc. aliquot was pippetted out and titrated with standard base from a 2cc. microburet. Concentrations of brosylates (all given at room temperature) were in the range from 0.02 to 0.07 mol./l. and titrations in acetic acid were carried out with a 0.05N standard solution of AcONa in acetic acid with Bromophenol Blue as indicator, and in ethanol, a 0.05N standard aquous solution of NaOH was used for titration with phenolphthalein as indicator. Rate constants were calculated from the formula

$$k_1 = 1/t \cdot \ln a/(a-x)$$

in which a was the initial concentration of brosylate and x was the concentration of sulfonic acid at time t.

The author expresses his sincere thanks to Professor Y. Tsuzuki for his advice and to Mr. M. Watanabe who prepared the diols used as starting materials.

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2) H. L. Goering and R. L. Reeves, *J. Am. Chem. Soc.*, **78**, 4931 (1956).
3) N. A. Milas and S. Sussman, ibid., **59**, 2345 (1937).
4) Organic Synthesis, Vol. 28, p. 35 (1948).
5) N. Mori, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **80**, 1458 (1959).

SHORT COMMUNICATIONS

Reaction of DL-*Threonine with Recoil Tritium Atoms*

By Yoshishige SATO, Teruhiko MESHI and Tadao TAKAHASHI

(Received April 28, 1960)

Using recoil tritium atoms from the $^{6}Li(n, \alpha)$ ^{3}H reaction, the studies on preparation of tritium labeled organic compounds have been carried out by Wolfgang[1], Rowland[2,3] and other investigators. In 1959, Kay, Malson and Rowland[4] investigated recoil tritium reaction with L-alanine having asymmetric carbon atom. They described that the tritium activity which is found on the α-carbon is, within error, all in the L(+) form the substitution reaction proceeds with retention of configuration, and no racemization or inversion occurs. This result is in accord with the essential absence of labeled galactose in irradiated crystalline glucose[5]. We have carried out the same experiments using DL-threonine and found the isomer (allo form) of it. The procedure is as follows.

A mixture of 2 g. DL-threonine and 1 g. lithium carbonate was irradiated with thermal neutron for 17 hr. at flux 2.5×10^{11} n/cm^2 sec. After irradiation the mixture was somewhat brownish. It was dissolved in water. To the aqueous solution was added basic copper carbonate. After filtering off the unchanged basic copper carbonate, the filtrate was concentrated in vacuo. Alcohol was added and thus crystals of amino acid copper salt were obtained. This amino acid copper salt was dissolved in water and to the solution an aqueous solution of hydrogen sulfide was added until the blue color disappeared. The precipitated cupric sulfide was removed by filtration, and the filtrate was concentrated. By the addition of alcohol to the concentrated solution, white crystals were obtained with yield of 800 mg. (sp. act. 0.113 μc/mg.).

Paper chromatography of the crystal using *n*-butanol-acetone-concentrated ammonium hydroxide-water (50 : 6.3 : 6.2 : 37.5, upper phase) as developing solvent showed three spots on spraying with ninhydrine. R_f values of three spots were identical with those obtained by pure DL-threonine (0.24), allo-threonine (0.17) and glycine (0.05), respectively. The product (120 μg.) was employed as sample of paper chromatography, and DL-threonine, allo-threonine and glycine were obtained in the amounts and with activity values as shown in Table I.

TABLE I. SPECIFIC ACTIVITY OF VARIOUS AMINO ACIDS SEPARATED FROM IRRADIATED DL-THREONINE

	Activity (cpm)	Amount (μg.)*	Sp. act. μc/mg.
DL-Threonine	961	65	0.082
allo-Threonine	138	7	0.108
Glycine	80	40	0.011

* Paper chromatographic yield from 120 μg. of the irradiated product.
** Approximate calculation.

In order to determine whether or not the inversion occurs at neutron irradiation, the blank test of the chemical purification described above was carried out, but allo-threonine was not detected. Under the consideration that DL-threonine is heated in the atomic reactor, the mixture of DL-threonine and lithium carbonate was heated at about 70°C for 17 hr. in an electric oven. However, in this experiment, allo-threonine could not be discovered.

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1) D. S. Urch and R. Wolfgang, *J. Am. Chem. Soc.*, **81**, 2025 (1959).
2) F. S. Rowland and R. Wolfgang, *Nucleonics*, **14**, (8) 58 (1956).
3) J. K. Lee, B. Musgrave and F. S. Rowland, *J. Am. Chem. Soc.*, **81**, 3803 (1959).
4) J. G. Kay, R. P. Malsan and F. S. Rowland, *J. Am. Chem. Soc.*, **81**, 5050 (1959).
5) H. Keller and F. S. Rowland, *J. Phys. Chem.*, **62**, 1373 (1958).

Evolution of Atomic Oxygen from Platinum Surface Treated Previously with Nitrous Oxide

By Kazuo Mitani and Yoshio Haranō

(Received July 5, 1960)

In the previous paper[1], it was reported that atomic oxygen is given off when nitrous oxide is decomposed by the platinum catalyst at low pressures ($1\times10^{-3}\sim5\times10^{-4}$ mmHg) by means of the flow method. When the pressure of nitrous oxide is higher (10~50 mmHg), no atomic oxygen is detected in a similar experiment. But evolution of atomic oxygen is detected in vacuo from heated platinum surface treated previously with nitrous oxide at pressures of 10~50 mmHg. The apparatus used is the same as reported in the previous paper[1]. Atomic oxygen given off is detected by the change of color of molybdenum trioxide deposited on a glass plate. Nitrous oxide is introduced into the reaction vessel to an initial pressure of 10~50 mmHg, and the platinum ribbon is heated to 1100°C. After 30 min., the nitrous oxide is considerably decomposed. In this procedure, molybdenum trioxide does not change its color. Then the reaction vessel is evacuated, by a diffusion pump, and, being continuously evacuated, the platinum ribbon is heated to 1400°C. In this case, molybdenum trioxide in the side tube changes its color from pale yellow to deep blue within 30 min. The platinum ribbon thus treated keeps its ability to change the color of molybdenum trioxide even after heating in vacuo at 1400°C for several hours. During the several experiments repeated, a dark brown film is gradually deposited on the glass wall of the reaction vessel. This dark brown substance seems to be not platinum metal, but platinum oxide[2], because it can mostly be dissolved by hydrochloric acid.

Instead of nitrous oxide, air is introduced into the reaction vessel to a pressure of 1 mmHg, and the platinum ribbon is heated to 1100°C for 30 min. After the apparatus being evacuated, the ribbon is heated to 1400°C in vacuo. Molybdenum trioxide does not change its color throughout this experiment. It is concluded from this that oxygen atoms chemisorbed on platinum surface are desorbed as molecular oxygen when heated in vacuo. The first step of the decomposition of nitrous oxide by the platinum catalyst has been believed to be

$$N_2O \rightarrow N_2 + O_{ads}$$

These adsorbed oxygen atoms may dissolve into the interior of the platinum metal, but then they may be evolved gradually in molecular form when heated after evacuation.

In the previous paper[3] it was reported that evolution of atomic oxygen is detected in vacuo from platinum surface treated previously with discharged oxygen gas. The platinum ribbon treated with nitrous oxide behaves in the same manner as the one treated with discharged oxygen, so it is concluded that platinum dioxide PtO_2 is also formed on the platinum surface treated with nitrous oxide, and that this platinum dioxide is the source of atomic oxygen.

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1) K. Mitani and Y. Haranō, This Bulletin, **32**, 1386 (1959).
2) Cf. E. K. Rideal and O. H. Wansbrough-Jones, *Proc. Roy. Soc.*, **A123**, 202 (1929); G. C. Fryburg, *J. Chem. Phys.*, **24**, 175 (1956).
3) K. Mitani and Y. Haranō, This Bulletin, **33**, 276 (1960).

Estrogenic Biphenyls. IX[1]*. Optical Resolution and Estrogenic Activity of 4'-(1-Hydroxypropyl)-4-methoxybiphenyl*

By Takeo Sato, Ken-ichi Sasamori and Michinori Ōki*

(Received July 5, 1960)

As reported in the preceding paper of this series[1], (4'-1-hydroxypropyl)-4-methoxybiphenyl (I) was moderately estrogenic when injected subcutaneously to ovariectomized mice. Since the location of the hydroxyl group attached to the asymmetric carbon atom in compound I corresponds to that of C_{17}-OH of estradiol (II) when the former is regarded as an aromatized BD-ring-lacking model of the latter, it has become of particular interest to examine the estrogenic activity of optically active form of compound I in comparison with the activities of epimeric estradiols, of which 17-β isomer represents more active form, being about 40 times more active than 17-α isomer.

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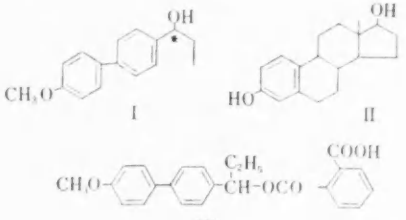
1) Part VIII: T. Sato, This Bulletin, **33**, 5 (1960).

(±)-4′-(1-Hydroxypropyl)-4-methoxybiphenyl (I)[1] was treated with phthalic anhydride in pyridine to produce (±)-4′-(1-hydroxypropyl)-4-methoxybiphenyl hydrogen phthalate (III), m. p. 164~165°C (Found: C, 76.64; H, 5.50. Calcd. for $C_{23}H_{21}O_5$: C, 76.58; H, 5.44%). It was converted into strychnine salt, which afforded a well crystallized optically active salt, m. p. 187~188.5°C (Found: N, 3.86. Calcd. for $C_{45}H_{44}N_2O_7$: N, 3.86%) with $[\alpha]_D^{15}$ −69.0° (*C*=2, 95% ethanol) through several recrystallization from ethanol. Combined mother liquors contained an oil which resisted attempts to induce crystallization.



III

The crystalline strychnine salt was treated with dilute hydrochloric acid to produce (+)-III, m. p. 149~153°C (Found: C, 76.10; H, 5.45. Calcd. for $C_{23}H_{21}O_5$: C, 76.58; H, 5.44%) having $[\alpha]_D^{17}$ +24.9° (*C*=2, 95% ethanol). Levorotatory alcohol (−)-I, m. p. 99~101.5°C (Found: C, 79.42; H, 7.65. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49%) with $[\alpha]_D^{14}$ −23.7° (*C*=2, 95% ethanol) was thus produced by the alkaline hydrolysis of (+)-III.

An attempt to obtain another alcohol with the opposite sign of rotation through cinchonine salt of the hydrogen phthalate III, m. p. 153~155.5°C, obtained by the hydrolysis of the oily strychnine salt mentioned above, failed owing to the unfavorable crystallizability of the salt.

Compound (−)-I, which was found to be active only in 20% of the test animals (ovariectomized mice) at the does of 200 γ, had weaker estrogenic activity than (±)-I as the latter was active in 80% of the animals at the same level[1]. Although the reason why dextro- and levorotatory 3,4-bis-(*p*-hydroxyphenyl)-hexanes show different estrogenic potencies[2] is still obsure, the present finding which suggests that the levorotatory isomer is the poorer estrogen may be attributed to the absolute configuration about the carbon atom which carries the hydroxyl group.

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2) F. v. Wessely and H. Welleba, *Ber.*, **74**, 777 (1941).

Absorption Spectra of Methylene Blue Adsorbed on Homoionic Bentonites Suspended in Water

By Choei Sato

(Received June 18, 1960)

The changes of the spectra of dyes added to some colloidal solutions are well-known as metachromasy. When some powdered materials usually used as adsorbents are suspended in water and dye solutions are added to them, color changes of the dye are also frequently observed if the dyes have the possibility ready to be adsorbed by those materials. In order to investigate if any relations exist between the trend of color changes of the dyes adsorbed and the surface structures of powdered materials used, the experiments have been carried out by using some kinds of clay minerals and silica gel, etc.[1] An interesting phenomenon has been observed in montmorillonite-methylene blue system; that is, the spectrum of the dye adsorbed on montmorillonite changes gradually with lapse of time after mixing of them. Furthermore this color change is influenced remarkably according to the kinds of added cation[2]. In order to clarify this phenomenon more thoroughly, the absorption

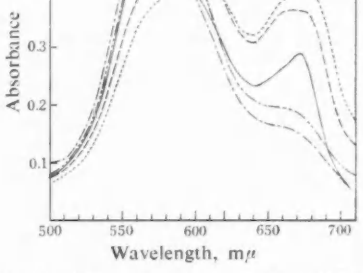

Fig. 1. Absorption spectra of methylene blue adsorbed on homoionic bentonites, after an hour from mixing.
—— Na-; -·-·- Ca-; ···· H-; ---- K-; ------ NH_4-bentonite

1) C. Sato, "Advances in Clay Science" Vol. 2, Edited by the Clay Research Group of Japan, Gihodo, Tokyo (1960), p. 69.
2) C. Sato, ibid. Vol., 3, in press; N. E. Vedeneeva, *Chem. Abstr.*, **49**, 4405b (1955).

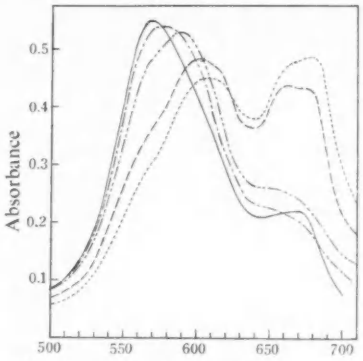

Fig. 2. Absorption spectra of methylene blue adsorbed on homoionic bentonites, after 2 days from mixing.
—— Na-; -·-·- Ca-; ···· H-; —— K-; ------ NH_4-bentonite

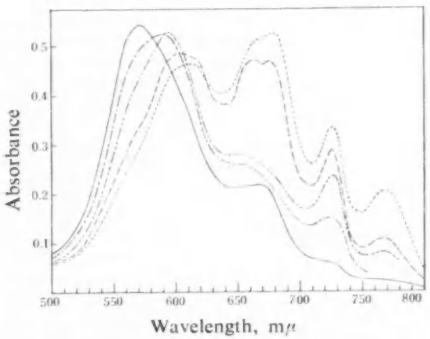

Fig. 3. Absorption spectra of methylene blue adsorbed on homoionic bentonites, after 7 days from mixing.
—— Na-; -·-·- Ca-; ···· H-; —— K-; ------ NH_4-bentonite

spectra of methylene blue adsorbed on homoionic bentonites suspended in water and having exchangeable cations of hydrogen, sodium, potassium, ammonium and calcium, have been observed.

Homoionic bentonite suspensions were prepared according to the method of Slabaugh, etc.[3] In each run 10 ml. of this suspension (0.13%) was divided into two equivalent parts, to one of which was added 0.5 ml. of the dye solution of a definite concentration, 1.74×10^{-4} mol./l., and to the other was added the equivalent amount of distilled water. Then the absorption spectrum of the former was measured with reference to the latter with a spectrophotometer, after about an hour from the addition of dye. Furthermore, the change of spectrum of the above system with longer lapse of time was also examined. The results obtained are indicated in Figs. 1, 2 and 3.

As seen in the figures, in potassium and ammonium bentonites, the band at 570 mμ decreases its intensity remarkably, and the broad bands at 600~620 mμ and 660~680 mμ, especially the latter, increase their absorbance markedly, with lapse of time. The bands at 725 mμ and 770 mμ become also apparent gradually. But in hydrogen and calcium bentonites the above change appears considerably slowly and in sodium one any change is scarcely observed in the spectrum which shows a strong band at 570 mμ and a weak one at 670 mμ. According to the view reported in literature[4] for the interpretation of absorption spectrum of methylene blue dissolved in water, it may be presumed that in ammonium and potassium clays a greater part of dye adsorbed initially in associated form on the outer surface of clay particle migrates easily to the firm binding of the unassociated dye ion on the interlayer surface, but in sodium, calcium and hydrogen clays, especially in sodium type, this migration is impeded. It is also assumed that these differences by the kinds of exchangeable cations may result from the correlation between the arrangement of water molecules adsorbed on interlayer surface and surrounding the hydrated cation, and the size of methylene blue ion. But any quantitative interpretation has not been attempted yet. The interpretation of appearance of the bands at 725 and 770 mμ has also been left unsolved.

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3) W. H. Slabaugh and R. H. Siegel, *J. Phys. Chem.*, **60**, 1105 (1956).

4) M. Schubert and A. Levine, *J. Am. Chem. Soc.*, **77**, 4197 (1955).

Synthesen von N-(4-Pyridyl)glycine

Von Masaki OHTA und Mitsuo MASAKI

(Eingegangen am 6. Juli, 1960)

Bei der Umsetzung von 3-Aminopyridin und 2-Aminopyridin mit Bisulfitverbindungen von Aldehyden und Alkalicyanid wurden die entsprechenden Glycine, *N*-(3-Pyridyl)glycine[1] und *N*-(2-Pyridyl)glycine[2] erhalten.

Weiter durch diesen Methode haben wir aus 4-Aminopyridin *N*-(4-Pyridyl)glycin und seine Derivate erhalten können.

Bei der Einwirkung von Bisulfitverbindung von Formaldehyd und Kaliumcyanid auf 4-Aminopyridin erhält man ein rotes Öl, das 4-Pyridylglycinnitril zu sein schient und beim Kochen mit Salzsäure *N*-(4-Pyridyl)glycin ergibt. Das letztere wird durch Einwirkung von Natriumnitrit in *N*-nitroso-*N*-(4-Pyridyl) glycin umgewandelt. Um 3-(4-Pyridyl)-sydnon darzustellen, versuchten wir Cyclisierung-Reaktion von der Nitrosoverbindung.

Wenn man die Nitrosoverbindung in Essigsäureanhydrid erwarmt, so erhält man farblose Nadeln von Schmp. 144~145°C, die aber nicht Sydnon, $C_7H_5O_2N_3$, sind. Sondern das Produkt zeigt sich durch Elementaranalyse eine Bruttoformel, $C_{10}H_{11}O_2N_3$, dessen Konstitution wir noch jetzt untersuchen.

In ähnlicher Weise reagiert 4-Aminopyridin mit Bisulfitverbindung von Benzaldehyd und Kaliumcyanid, und ergibt ein rotes Öl, woraus *N*-(4-Pyridyl)-phenylglycine durch Kochen mit Salzsäure dargestellt werden kann.

Beschreibung der Versuche

Salzsaures *N*-(4-Pyridyl)glycin. — Man versetzt 4 g von 37 proz. Formalin mit einer Lösung von 5.2 g Natriumbisulfit in 10 ccm Wasser, erhitzt 0.5 Std auf dem Wasserbad und darauf versetzt mit 4.7 g 4-Aminopyridin. Nach 1.5 std. Erhitzen und Umrühren setzt man dazu 3.5 g Kaliumcyanid in wenigem Wasser zu. Das Gemisch wird unter mechanischem Rühren 2 Std auf dem Wasserbad erhitzt, noch 1 Std bei Raumtemperatur umrührt und dann unter vermindertem Druck eingedampft. Der Rückstand wird mit Äthanol ausgezogen, nach dem Abdampfen des Äthanol ergibt die Lösung ein rotes Öl. Man löst das Öl in 30 ccm von 1 : 1 HCl, erhitzt auf dem Wasserbad und nach 3 std. Erhitzen läßt bei Raumtemperatur stehen, bald scheiden sich 2.8 g Nadeln ab. Aus die Mutterlauge erhält man noch 1.6 g Salzsäuresalz. Farblose Nädelchen von Schmp. 255~256°C (aus Wasser).

$C_7H_8O_2N_2 \cdot HCl$

Ber. C 44.56 H 4.77 N 14.85
Gef. C 44.28 H 4.94 N 14.86

***N*-Nitroso-*N*-(4-pyridyl)glycin.** — Man löst 3.7 g salzsaures *N*-(4-Pyridyl)glycin in 40 ccm Wasser, fügt langsam 1.6 g Natriumnitrit unter Eiskühlung und Umrühren hinzu und läßt im Eisschrank stehen. Nach 30 std. Stehen wird der ausgefallene farblose Niederschlag abfiltriert. Ausb. 3 g. Farblose Nädelchen vom Schmp. 202°C (aus Wasser) zeigen Liebermannsche Reaktion.

$C_7H_7O_3N_3$

Ber. C 46.41 H 3.90 N 23.20
Gef. C 46.56 H 4.14 N 23.22

***N*-(4-Pyridyl)phenylglycin.** — Zur Lösung von 10.4 g Natriumbisulfit in 40 ccm Wasser gibt man 10.6 g Benzaldehyd, erhitzt 1 Std auf dem Wasserbad und dann fügt 9.4 g 4-Aminopyridin hinzu. Nach 2 std. Erhitzen setzt man dazu 7 g Kaliumcyanid gelöst in 20 ccm Wasser zu und rührt 2 Std bei Raumtemperatur und dann 0.5 Std auf siedendem Wasserbad. Das abgeschiedene gelbrote Öl wird mit Chloroform ausgeschüttelt und mit Natriumsulfat getrocknet. Das nach dem Abdampfen des Chloroforms zurückbleibende rote Öl löst man in 70 ccm von 1 : 1 HCl, erhitzt 4 Std auf dem Wasserbad und dann läßt die Lösung bei Raumtemperatur stehen. Nach einer Nacht wird der ausgefallene Niederschlag abfiltriert, im Wasser gelöst und dann mit Natriumbicarbonat neutralisiert. Bald fällt ein farblose Niederschlag aus, der zusammen mit dem durch Neutralisierung von die erste Mutterlauge erhaltenen Niederschlag aus Wasser in Nadeln vom Schmp. 240°C umkristallisiert wird, die zur Analyse 4 Std bei 100°C in Vakuum getrocknet wird.

$C_{13}H_{12}O_2N_2$

Ber. C 68.41 H 5.30 N 12.27
Gef. C 68.71 H 5.57 N 12.44

Herrn Asaji Kondo danken wir bestens für seine Ausführung der Mikro-analyse.

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1) M. Ohta und M. Masaki, Dieses Bulletin, 33, 649 (1960).
2) M. Ohta und M. Masaki, ebenda, 33, im Druck.